MILITARY MEDICINE

Formerly:
THE
ILITARY
URGEON

UNIVERSITY OF MICHIGAN
APR 15 1956
MEDICAL LIBRARY

DOES NOT CIRCULATE

Washington, D.C.

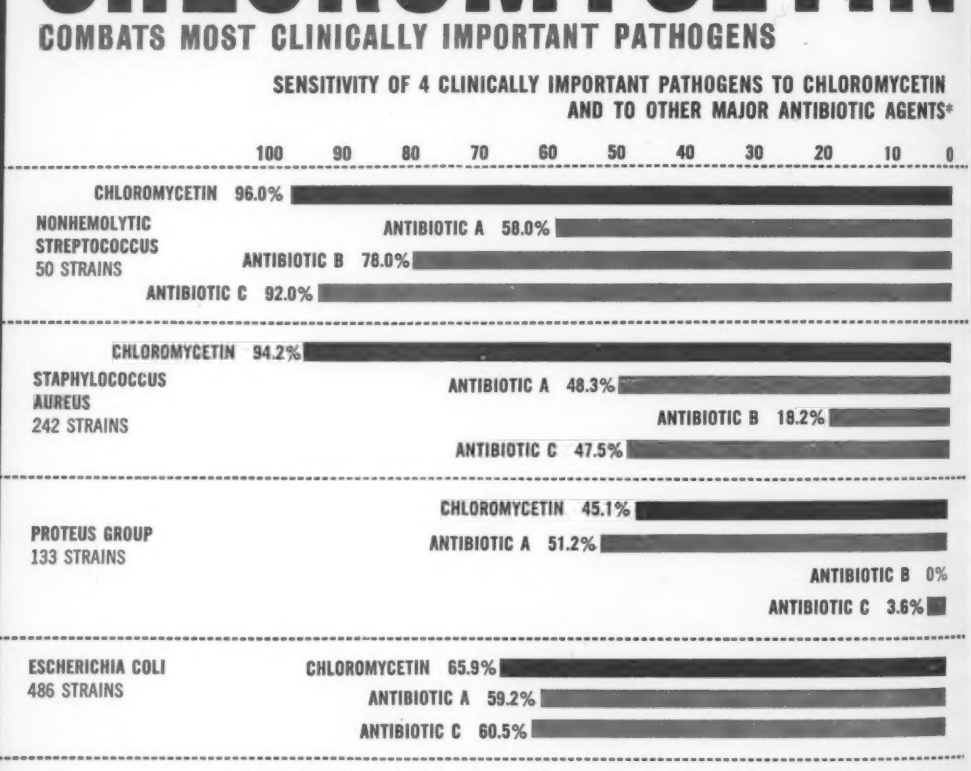
VOL. 120 APRIL 1957 NO. 4

64TH ANNUAL CONVENTION, HOTEL STATLER,
WASHINGTON, D.C., OCTOBER 28-30, 1957

CONTINUING ANTIBACTERIAL EFFICACY CHLOROMYCETIN®

COMBATS MOST CLINICALLY IMPORTANT PATHOGENS

SENSITIVITY OF 4 CLINICALLY IMPORTANT PATHOGENS TO CHLOROMYCETIN AND TO OTHER MAJOR ANTIBIOTIC AGENTS*



*This graph is adapted from Rantz, L. A., & Rantz, H. H.: *Arch. Int. Med.* 97:694, 1956. It is based on *in vitro* studies of bacteria freshly isolated from clinical materials.

CHLOROMYCETIN (chloramphenicol, Parke-Davis) is a potent therapeutic agent and, because certain blood dyscrasias have been associated with its administration, it should not be used indiscriminately or for minor infections. Furthermore, as with certain other drugs, adequate blood studies should be made when the patient requires prolonged or intermittent therapy.

PARKE, DAVIS & COMPANY · DETROIT 32, MICHIGAN

50109

VOL. 120 April, 1957 NO. 4

MILITARY MEDICINE

(*Formerly* THE MILITARY SURGEON)

Official Publication · Association Military Surgeons of the United States

President:
COL. AMOS R. KOONTZ
MC, Md., NG

Editor:
COL. ROBERT E. BITNER
U. S. Army Ret.

Published monthly and constituting two volumes annually.
Volumes commence with the January and July numbers.

Copyright ©, Association of Military Surgeons of U.S., 1957.

Contents

Original Articles, Postgraduate Seminar, Armed Forces Institute of Pathology, May 14-17, 1956.

Opening Address 247
William M. Silliphant, Capt. (MC), USN

The History of Cardiology—An Outline Sketch 250
Morris C. Leikind

The Histology of the Heart and Its Changes with Age 257
Maurice Lev, M.D.

The Conduction System in the Human Heart 262
Maurice Lev, M.D.

The Anesthetic Management of the Patient with Heart Disease 269
Timothy G. Barila, Major MC, U. S. Army

Glycogen Disease 276
Walter G. J. Putschar, M.D.

Clinical Aspects of Rheumatic Heart Disease 282
W. Proctor Harvey, M.D.

Pathology of Rheumatic Heart Disease 289
Ira Gore, M.D.

Clinical Aspects of Coronary Arteriosclerosis 296
Byron E. Pollock, Col. MC, U. S. Army

Surgical Aspects of Coronary Arteriosclerotic Heart Disease 302
Morris H. O'Dell, M.D.

Vascular Lesions Associated with Heart Disease 310
William C. Von Glahn, M.D.

Editorial 312

Around the World—Claudius F. Mayer, M.D. 313

Sustaining Members 316

Association Notes 317

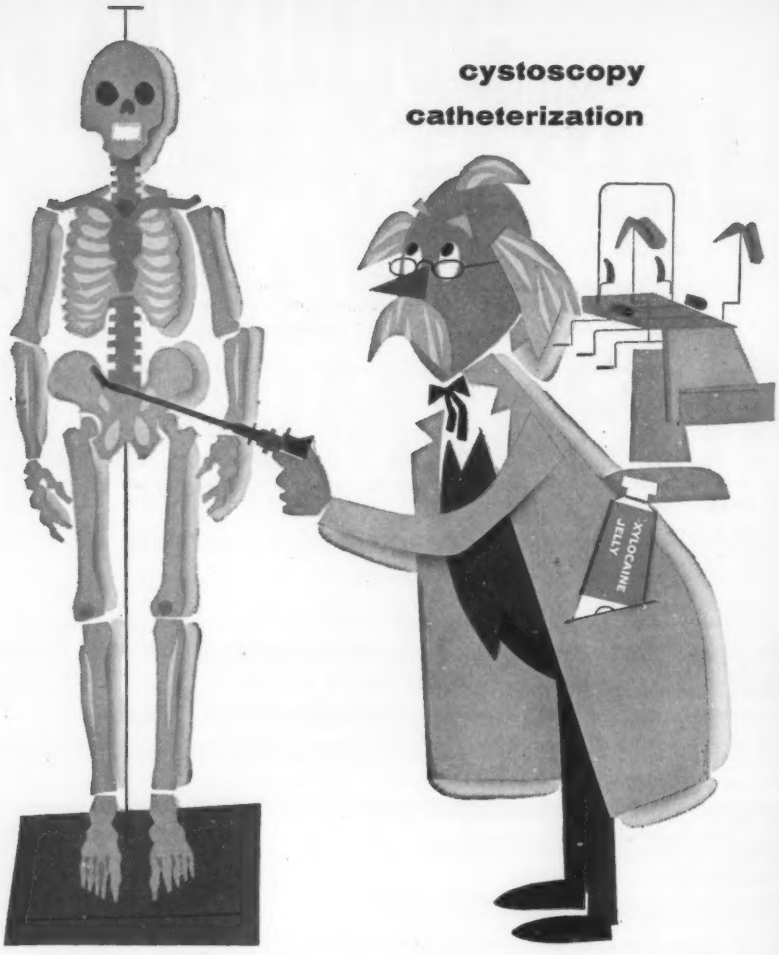
Obituaries 326

Book Reviews 327

New Books 328

Index to Advertisers 8b

• Entered as second class matter at the post office at Washington, D.C., with additional entry at Menasha, Wisconsin. • Acceptance for mailing at special rate of postage provided for in paragraph 4, section 538 P. L. & R., authorized April 14, 1926. • Publication office: 450 Ahnaip Street, Menasha, Wisconsin. • Editorial and Executive Office: Suite 718, New Medical Building, 1726 Eye St. N.W., Washington, D.C. • Advertising Representative: 280 Madison Ave., New York 16, N.Y. • Subscription $7.50 a year for the United States. Elsewhere throughout the world, $8.50. Current copy, 75 cents. Subscriptions payable in advance. Membership dues (including subscription to MILITARY MEDICINE) $6.00. Checks should be made payable to The Association of Military Surgeons, U.S., and not to any officer personally. • *The addresses of members and subscribers are not changed except upon request.* In every case the old as well as the new address should be given. Requests for change of address must reach the Secretary before the fifteenth of the month to be effective for the following issue. • Requests for reprints should be made at the time of forwarding article. Authors alone are responsible for the opinions expressed in their contributions. Printed in U.S.A.



. . . Xylocaine Jelly is the ideal topical anesthetic for rapid, sustained relief and relaxation during painful urethral procedures. Its nonstaining, water-soluble base adheres instantly and intimately to urinary mucosa. Nonirritating and nonsensitizing; facilitates instrumentation by lubricating as it anesthetizes.

Astra Pharmaceutical Products, Inc., Worcester 6, Mass., U.S.A.

for better doctor-patient relationship

XYLOCAINE®
(brand of lidocaine*)
JELLY ASTRA

U.S. PATENT NO. 2,441,498

VOL. 120 April, 1957 NO. 4

MILITARY MEDICINE

ORIGINAL ARTICLES

Authors alone are responsible for opinions expressed in their contributions

Diseases of the Heart*

Postgraduate Seminar Held at The Armed Forces Institute of Pathology, Washington, D.C., May 14-17, 1956. Co-sponsored by The American Heart Association, Inc.

Opening Address

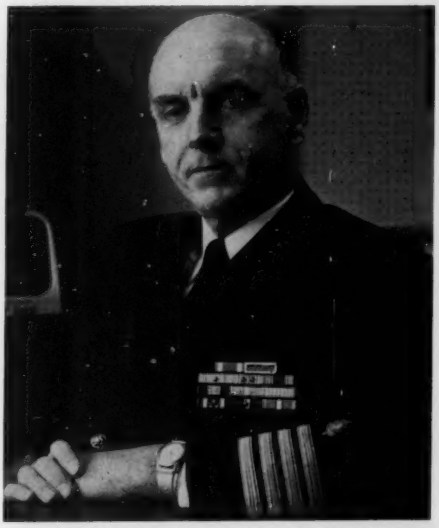
By

CAPTAIN WILLIAM M. SILLIPHANT, *Medical Corps, U. S. Navy,*
Director of the Armed Forces Institute of Pathology

IT IS a pleasure to welcome you to this postgraduate seminar on "Diseases of the Heart."

This is a pioneer attack on this particular subject for the Armed Forces Institute of Pathology. It was inspired by an idea conceived last fall, when Doctor W. C. Manion, your Course Director, attended the meeting of The Registry Committee of the American Heart Association in New Orleans. After he returned his infectious enthusiasm for the project rapidly spread to other members of the Staff. Soon we found ourselves committed and today the seminar is a reality.

We are delighted to see such a large attendance. It is indicative of the high interest this subject presently commands. This class consists of approximately 350 doctors, with representatives from all over the United States. Approximately fifty percent of you are from civilian medical practice. It is most gratifying to act as host to such a group as this, representing all the military services, other Federal Agencies, and civilian medicine.



CAPT. WILLIAM M. SILLIPHANT, MC, USN, DIRECTOR, ARMED FORCES INSTITUTE OF PATHOLOGY

Heart disease in this country today is called by some a "major American worry" or "the typical American illness." Perhaps there is some basis for the concern that by prolonging the life span with modern methods of therapy, heart disease is becoming more prevalent. In any case, it is blazoned in today's headlines as the nation's number

* Some of the papers delivered at the Seminar are presented in this issue of MILITARY MEDICINE. Editor.

AFIP

WM. C. MANION, M.D., CHIEF, CARDIOVASCULAR PATHOLOGY, ARMED FORCES INSTITUTE OF PATHOLOGY *(Seminar Director).*

one killer. Yet only yesterday, I noted that insurance surveys report a slight decline in heart disease deaths in the past 20 years. Perhaps, because more precise and accurate diagnoses are now being made, we are just more conscious of heart disease.

Though deaths from this cause still lead all others in the United States, that is not the case in all countries. It is certainly not true in any country on the Continent of Asia.* There the top killers are epidemic diseases and others such as tuberculosis, malaria, beri-beri and cancer. The highest rate of heart disease death in Asia is found in Japan, where it ranked as fifth most frequent cause of death, with a rate of only 59.8 per 100,000. In the United States in 1953 the rate was 501.4 per 100,000. Why this wide difference in statistics? Is it due to diet, environmental factors, or way of life? Some day undoubtedly the answer will be found.

Despite the high incidence, however, the patient with heart disease no longer lives the restricted life of a frustrated invalid. For the most part he continues to fill his niche in work and society, and frequently leads a more or less normal life. Millions of dollars are now spent for research on cardiovascular diseases. Methods of treatment, both medical and surgical, have undergone radical changes in recent years. Surgical procedures on the heart and blood vessels, which today are routine, seemed fantastic only a few short years ago. To hear about these new advances in diagnostic and therapeutic measures, you are here.

In looking over the list of names on the faculty, I am assured that you will find the next four days well worth your while. In addition to certain members of our own staff, and that of the Walter Reed Army Medical Center, you will note that we drew heavily on experts from other institutions, not only in Washington, but throughout the country. Their names are recorded on the program which you have been given. One-half of them are from civilian medical teaching institutions. We are deeply indebted to these participants who arranged their busy schedules to come here for this purpose.

Short courses of this nature are offered from time to time at the Armed Forces Institute of Pathology, but their subject matter is generally limited to special phases of pathology, which for the most part, are not adequately covered in medical schools or by postgraduate education. This particular seminar on heart disease is somewhat out of the ordinary for the AFIP, for it is not confined to pathology, but is designed to familiarize the clinician, the radiologist, the surgeon, and the pathologist with recent advances in the field of cardiovascular disease. Practically all specialties in medicine and surgery are represented among you. As you will see, the material will be presented from various aspects, such as the anatomical, clinical, radiological, surgical, as well as the pathological. Experts in each of these fields will be your teachers. I am told that this is the first time that an intensive course in heart disease of this scope and nature has been offered and presented in this fashion.

The courses given by the AFIP as many

* *Science,* volume 124, no. 3211, page 69.

of you know, are open to military and civilian doctors alike. In general, they have been heavily oversubscribed by interested applicants. In some of these courses, because the use of the microscope is required, the enrollment is limited to 50. That restriction is not imposed in this course, which, from the standpoint of enrollees, is the largest we have ever had. Our AFIP auditorium has not the capacity to accommodate you, and that is why we are in this Post theatre, with the kind permission of Major General Leonard Heaton, Commanding General, Walter Reed Army Medical Center. We would like to think, however, that you are primarily the guests of the AFIP, whose new building is located just across the street from here.

No other military activity is more closely affiliated with civilian medical practice than the AFIP. This association is made possible through the American Registry of Pathology, one of our four major professional departments. To the Registry any civilian doctor in the country, through his pathologist, may send pathologic specimens of teaching and research value. The large accumulation of well selected and documented cases in the Registry are available for study and research to any qualified military or civilian doctor.

The Cardiovascular Registry, in which you here would be most interested, was organized in 1948, and is sponsored by the American Heart Association. You will note on your program that the latter organization is a co-sponsor of this seminar. In the eight years of its existence, about 1,600 cases have been registered in the Cardiovascular Registry, 52 percent of which have been contributed by the Armed Forces, 25 percent by the Veterans Administration, and 23 percent by civilian physicians. Doctor Manion, the Registrar, would be grateful for contributions of more good teaching material from doctors throughout the country. At present he is particularly interested in congenital anomalies and he probably will tell you more about this later.

Gentlemen, again let me say it is indeed an honor to have you as guests of the AFIP for the next few days. I hope you will find this seminar interesting and stimulating and that when you depart from here, you will feel that your time has been well and profitably spent.

U. S. Air Force Photo

COL. FRANK M. TOWNSEND, USAF (MC), DEPUTY DIRECTOR, ARMED FORCES INSTITUTE OF PATHOLOGY.

U. S. Army Photo

COL. JOE M. BLUMBERG, MC, USA, DEPUTY DIRECTOR, ARMED FORCES INSTITUTE OF PATHOLOGY.

The History of Cardiology—An Outline Sketch*

By

MORRIS C. LEIKIND

Chief, Historical Research Division, Medical Museum, Armed Forces Institute of Pathology, Washington, D.C.

THE history of cardiology epitomizes in a sense the history of medicine since the knowledge, the arts and skills required to develop this specialty are those which have advanced medicine itself.

When does our knowledge of cardiology begin? When man first became aware of the heart. We cannot fix an exact date for this but we know that our pre-historic ancestors recognized the importance of the heart since they have left us drawings of it. These pictures on the walls of certain caves in Europe show animals with the heart clearly delineated—presumably to show a primitive hunter his vital target. Some of these paintings are at least 20,000 years old.

As we come to the dawn of recorded history we find references to the heart and pulse in some of the earliest medical texts which survive. Notable among them are the Edwin Smith Surgical Papyrus and the Ebers Papyrus both of which were written around the 16th or 17th centuries B.C. and appear to be copies of material from about 3000 B.C. One of the references to the heart reads —"his heart is too weary to speak." In another passage the probing fingers of the physician find a "fluttering and throbbing like that on the crown of an infant's head before it has grown together." That the early Egyptians considered the heart an important vital organ is plain from the fact that during the rite of mummification the heart was left in the body while the brain was destroyed. Yet on the basis of available evidence it cannot be assumed that the ancient Egyptians or the Assyro-Babylonians had any knowledge or understanding of the circulation. As a matter of fact their knowledge of both anatomy and physiology was most rudimentary, based as it was, not upon systematic dissection and experiment, but rather on casual observations made principally in the butcher shop and the sacrificial altar. Medicine in its very early beginnings was too much immersed in magic and superstition to have a firm scientific base.

Centuries later, the Greeks, especially those associated with the school of Hippocrates took the first tentative steps to separate medicine from magic. Hippocrates and also Aristotle regarded the heart as the most important organ of the body, the center of life and the seat of intelligence. In general, the heart was looked on by the Greeks as an organ of bodily heat and the brain as an organ for cooling the blood. Hippocrates believed the heart to be immune to disease.

About 300 B.C. when the Greek center of medical study shifted to Alexandria two figures stand out—Herophilus and Erasistratus. The former, an anatomist, showed that the brain and not the heart is the seat of intelligence. He distinguished between arteries and veins. Erasistratus came close to discovering the circulation. He regarded the heart as a pump—he examined its valves and the chordae tendinae. However, like Herophilus he believed that arteries carried air, the veins blood. Four hundred years later—Galen, the greatest physician and experimental physiologist of antiquity—after Hippocrates—showed that arteries do contain blood and not air as Herophilus and Erasistratus had claimed. This he did by the simple experiment of ligating an artery in two places and cutting the vessel between the ligatures. Nevertheless, Galen was not a

* The substance of a lecture at the Post-Graduate Seminar on Diseases of the Heart, sponsored jointly by the Armed Forces Institute of Pathology and the American Heart Association, Inc. and held at the Walter Reed Army Medical Center, May 14-17, 1956.

modern scientist and his speculations went far beyond the limits imposed by his observations and experiments. His most famous and most lasting physiological theory is that concerning the flow of the blood—a concept which dominated medical thought and put an effective brake upon its progress for well over a thousand years. According to Galenic doctrine nutritive material went from the intestine to the liver where it was transformed into blood and acquired pneuma or natural spirit. From the liver it ebbed too and fro in the veins. Some of this blood entered the heart and into the lungs there to be purified. But the rest went into the left side of the heart through pores in the septum. In the process it acquired vital spirit and went through arteries to the brain to become animal spirit—this latter being distributed by way of the nerves—believed to be hollow. Let us not laugh at this doctrine. It persisted for centuries—yet it was the best that our ancestors could do with the knowledge at their disposal. Thus it was not until the Renaissance, that period of almost explosive intellectual awakening that at long last the dead hand of authority was removed from the wheels of progress. It was in the fifteenth and sixteenth centuries that men like Leonardo da Vinci, Andreas Vesalius and a host of others whom time does not permit me to mention, began to see and describe what they were looking at and not what Galen and the ancients told them to see. From the hand of Leonardo da Vinci came the first accurate drawings of the heart and some experimental attempts to elucidate the movement of the heart by following the motions of long needles inserted through the chest wall into the still beating heart of a pig. Leonardo was also the first to describe the moderator bands of the heart.

But it was with Vesalius that the first steps were taken which led to the solution of the riddle of the circulation—a riddle of which Fracastorius had written "that the motion of the blood was to be apprehended only by God."

Leonardo's work had little influence since his writings and notes were not published until long after his death. But Vesalius was fortunate because when he appeared on the scene—the printing press was available to him. The invention of printing was an event of the very highest importance for the advancement of science and learning since it made possible the democratization of knowledge.

Courtesy of Doris Appel

WILLIAM HARVEY, M.D. (1578-1657)

When Vesalius published his classic work on the structure of the human body in 1543, he corrected many of Galen's errors—errors which arose from the fact that Galen's anatomy was largely pig anatomy—the anatomy of Vesalius was based on the human body. A major error corrected by Vesalius was the doctrine evolved by Galen that there were invisible pores in the interventricular septum and thus the blood went from the right to the left ventricles. Vesalius in his second edition flatly stated that he could see no pores and could not explain how the blood got from one side of the heart to the other. But he laid the structural foundation for discoveries to come. As a matter of fact—a major break-through was imminent. Already there were premonitory suggestions of this.

As early as the 13th century, an Arab scholar Ibn-an-Nafis—his work unknown until very recently—had described in unmistakable terms the lesser or pulmonary circulation. There is no present evidence that this work was known to Vesalius or any of his followers. In Spain, in 1553, Michael Servetus, a theologian also described independently the lesser circulation. Two years later Realdo Colombo who taught at Padua after Vesalius also described the pulmonary blood flow. Colombo worked at Padua, that fertile hot house of genius. In the same anatomic theater where Vesalius had dissected, worked Fabricius ab Aquapendente. It was he who published a classic work on the valves in the veins. The idea of a one way flow for the blood stream was now ready to be announced. But it was not Fabricius but his brilliant pupil William Harvey of England who finally fitted together almost all the pieces in the puzzle and demonstrated the fact that the blood moves in a circle propelled by the muscular force of the heart. This—the most important event in the history of cardiology was announced in a little booklet of 72 pages in 1628.

The book was entitled "Exercitatio Anatomica de Motu Cordi et Sanguinis in Animalibus" or *Anatomical Studies on the Motion of the Heart and Blood in Animals.* It was a masterful exposition and yet it did more, much more, than announce the fact of the circulation of the blood. For, what William Harvey did was to introduce the experimental method into biology and medicine. In these fields he gave us and showed us how to use, the most powerful tool we possess for investigating the secrets of life, of health, and disease. He showed us how to question nature and to extract and interpret her answers.

The year 1957 will mark the three hundredth anniversary of the death of William Harvey and it, therefore, seems appropriate to recall very briefly a few facts about his life and work. Born in Folkstone, England, on April 1, 1578, William Harvey was the eldest of a "week of sons." Five of his seven brothers became business men, a career which had no appeal for the scholarly William. He began his higher education at Cambridge and in 1597 after taking his B.A. he went to Padua in northern Italy to study medicine.

The school in Padua was then at the zenith of its glory. There Vesalius had taught and now Harvey found Fabricius ab Aquapendente—himself a student of Fallopius—in turn taught by Vesalius—occupying the chair of anatomy. At Padua, Harvey received not only a medical degree after brilliantly passing his examination but also the friendship of his teacher and the scientific stimulus which led to his great discovery.

Upon his return to England, Harvey established himself as a physician and surgeon and soon won appointment as Physician Extraordinary to King James I and then to a similar post under Charles I. In addition he served as Physician to St. Bartholomew's Hospital for 36 years. Thus we see that Harvey was not cloistered in a white ivory research tower. He was, in fact, an active man of affairs with a wide ranging inquisitive mind and the stubborn will and energy to accomplish his ends.

Despite the fact that he was known to be a voluminous writer, only two major works have survived: his *De Motu Cordis* and his *De Generatione,* the latter dealing with his studies on embryology. The bulk of his writings were burned by a mob during the London riots in the Civil War of 1642—a loss Harvey felt keenly and bitterly.

We turn now to his work on the circulation. We have already reviewed the status of the problem as it was when Harvey set his hand to it.

It is not possible to discuss in detail what Harvey did in solving the problem. As a matter of fact it is much better to read his own book. The translation prepared by Chauncey Leake in 1931 is excellent. The late Fielding H. Garrison describes the book thus: "To open the *De Motu Cordis* is to enter the laboratory of the ablest investigator of comparative anatomy and physiology

since Aristotle and Galen. To read it is like reading Beaumont's book of experiments on gastric digestion. Everywhere we are conscious that Harvey wishes to abandon speculation and actually tries to make us see how the heart works, how the blood flows in vivisected animals, even as Beaumont visualizes the interior of the stomach in situ through his accidental experiment in physiological surgery."

Harvey begins by pointing out the errors of his predecessors. Then he analyses the sequence of events in the cardiac cycle and shows that the heart is not a suction pump but rather a force pump. He goes on then to consider the effect of the pumping action on the arteries—the role of the contraction of the auricles in producing the heart-beat, heart-block, venous pressure. He studied the comparative anatomy and physiology of the blood flow into, through, and out of the heart; then comes his quantitative demonstration in which he calculates that during a given time interval the heart pumps out more blood than can be accounted for by ingested food, by the volume expelled through the arteries, and, finally, that the venous flow is only from every part of the body to the heart.

All of this and much more appears in this small book. Only one thing was lacking—the proof that the blood flows from the arteries to the veins through the capillaries. The microscope was already in existence but Harvey did not make use of it.

I said a moment ago that Harvey fitted together almost all the pieces in the puzzle of the movement of the blood. The missing link was the passage from arteries to veins. For Harvey, capillaries were a logical necessity. Two men, Marcello Malpighi, and Antony Van Leeuwenhoek, using that new instrument of biological research, the microscope, made capillaries a histological certainty. The circle was now complete.

And with the completion of the circle cardiology was about ready to appear as a science. Harvey had used quantitative methods in demonstrating the circulation. Another quantitative step of equally great significance

Courtesy National Library of Medicine

STEPHEN HALES, F.R.S. (1677-1761)

came in 1733 when Stephen Hales—an Anglican Curate who with his classic experiment measuring the blood pressure of the horse opened up hemo-dynamics as a branch of cardiology. He calculated the velocity of the blood flow in the aorta and showed that the pulse rate is more rapid in small animals than in large. Not until the time of Carl Ludwig who in 1847 introduced the mercury manometer was much added to this aspect of our knowledge of cardiology. But Harvey's discovery had other consequences. It provided the basis for explaining another mystery—that of respiration. These advances were made swiftly—many by men who were contemporaries of Harvey. Among them were Robert Boyle and Richard Lower. It was the latter who showed that fresh blood clots turned bright red when exposed to air. Boyle was the first to study the blood gases and also to note air embolism and its mechanical effects. Robert Hooke, Boyle's assistant then showed that the essential fact in respiration was the passage of air into and out of the lungs and not the motion of lungs per se. About a quarter of a century later—John Mayow suggested that a special part of the air was the essential element in respiration—

Courtesy National Library of Medicine

JOHN BAPTIST MORGAGNI, M.D. (1682-1771)

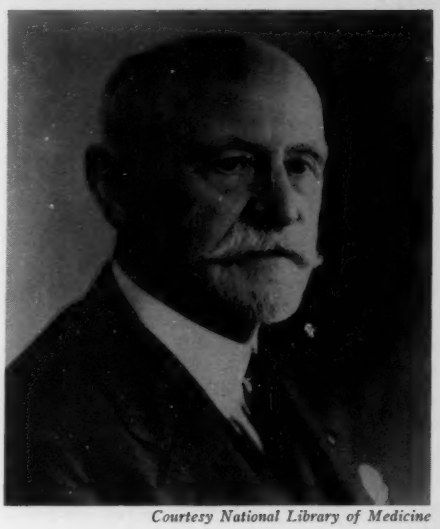
a suggestion culminating in the discovery of oxygen by Scheele, Priestley and explained and confirmed by Lavoisier in the eighteenth century.

But now another phase of cardiology comes to the fore. Until the time of William Harvey practically nothing was known about diseases of the heart and the circulation. Hippocrates himself as mentioned earlier considered the heart to be immune to disease. Here again we find that science advances in a step-wise and sequential fashion. For before we could have anatomy and physiology in the modern sense—men had to learn to think in anatomical and physiological terms. Thus—despite the fact that the ancients, the Egyptians—the Greeks—even the Chinese, knew of the pulse and even made attempts to count it—their knowledge was incomplete until 1628. For the pulse by itself explained nothing. And in the same way—until the beginnings of the Renaissance pathological anatomy was non-existent in the absence of accurate knowledge of normal anatomy. But when Vesalius had put anatomy on a rational basis then men began to look more closely at the manifestations of disease in the body.

One of the first to draw attention to diseases of the heart was Raymond Vieussens of Montpellier who in 1715 wrote a treatise on heart disease in which he described pericarditis, mitral stenosis and aortic regurgitation. Even before this, in 1707, Lancisi of Rome had written at the request of Pope Innocent XII—a treatise on Sudden Death—in which he attempted a classification of heart disease. In France, Senac in 1749 wrote an important book—on the heart, its action and diseases, which, well into the 19th century, was regarded as a standard work. He was one of the very first to use quinine in the treatment of heart disease. The most influential of the 18th century workers, however, was Morgagni who in 1761 (he was 79) published his classic work on seats and causes of disease. Now at last pathology acquired an anatomical basis. Published in the form of letters to a friend Morgagni organized and codified a vast number of miscellaneous observations on the lives and deaths of his patients. In his autopsy protocols may be recognized rupture of the heart, myocardial fibrosis, most of the valvular lesions, heart block and aortic aneurysm. It is interesting to note, incidentally, that Morgagni was the first to stress the importance of physical signs in the diagnosis of diseases of the chest. This was in 1761 the same year in which Auenbrugger published his classic on percussion, a book which was almost forgotten until Corvisart, Napoleon's physician translated it into French in 1808. But Corvisart did more than discover Auenbrugger. He was the teacher of Laennec, the inventor of the stethoscope, an instrument which has added so much to our knowledge of diseases of the chest and of the circulatory system.

Thus we see that by the opening of the 19th century—tremendous advances had been made. Not only was the theory of the circulation now an established fact, but respiration was beginning to be understood—metabolism was not quite the mystery it had been and many disease phenomena were recognized.

Heart disease was not quite the hopeless affliction it was considered to be when attention was first directed toward it. In 1785 William Withering introduced digitalis into cardiology and the hope was raised that other drugs might be found useful in diseases of the heart. About the same time William Heberden published his classic descriptions of angina pectoris although he had no notion of the cause. However, it was the sudden death of John Hunter of an attack of angina which focused more attention on this syndrome. Hunter himself had examined a case at post-mortem—a patient of John Fothergills—diagnosed as having angina. Hunter found a calcified coronary artery. Edward Jenner and Caleb Perry, however, were the pioneers of the coronary artery theory of the origin of angina. They had already noted the condition but withheld publication because they knew that Hunter, their teacher, was suffering from this disease. As a matter of fact, however, the recognition of the importance of the coronary arteries and their relation to heart disease did not come until the twentieth century, especially through the work of James Herrick of Chicago, who incidentally has written a good account of the history of coronary thrombosis. Another etiologic advance came when William Charles Wells around 1812 drew attention to the connection between rheumatism and cardiac disease.



Courtesy National Library of Medicine

JAMES B. HERRICK, M.D. (1861-1954)

Courtesy National Library of Medicine

RENÉ THÉOPHILE LAËNNEC, M.D. (1781-1826)

It was at this stage of cardiology that Laennec came with his stethoscope. Within a short time after its invention he published in 1819 his treatise on Mediate Auscultation in which he described and correlated the sounds heard, with symptoms in the clinic and anatomical findings at the autopsy table. True, he made errors but what pioneer doesn't? Who was there to correct him? Nevertheless—he did point the way to acquire new knowledge. His method of correlating symptoms with autopsy findings was most enthusiastically exploited in Vienna where it became a sort of game to see who could most accurately predict autopsy findings at the bedside. However, the stethoscope was not the only diagnostic tool for the study of heart and circulatory disorders. Thus, increased attention to the pulse by such men as Stokes, Adams, Cheyne, and Corrigan—physicians of the Irish School—did much to advance our knowledge. In 1867 Pierre Po-

tain brought the sphymograph out of the laboratory into the clinic. He showed how to make simultaneous records of the pulse, apex beat and the blood flow in the jugular vein. It was Sir James Mackenzie who developed this technique even further and placed the clinical study of heart disease on a more scientific basis.

The advent of bacteriology in the latter half of the 19th century added a new tool to the diagnostic armamentarium. Thus it now became possible to diagnose accurately such conditions as infective endocarditis. At almost the same time two new and significant diagnostic aids appeared. In 1895 Roentgen discovered the x-rays which were quickly applied as a diagnostic tool in medicine. One of the first to use the Roentgen rays in cardiology was F. H. Williams of Boston in 1906. In 1903 William Einthoven developed the string galvanometer for studying the electrical activity of the heart and Sir Thomas Lewis, Mackenzie's greatest pupil, brought this technique into the clinic. With the advent of the electrocardiograph we reach the modern period of cardiology.

There were of course many other developments which I wish I had time to mention such as the development of cardiovascular surgery, the advent of transfusion, the influence of pharmacology on cardiology especially since this year marks the centennial of the discovery of aniline dyes and opened up the exploitation of coal-tar as a source of vast numbers of chemicals including drugs as well as dyes. The new dyes came at the moment when they could be applied to the development of cytology and histology and to the concept of cellular pathology announced by Rudolph Virchow in 1858. The aniline dyes were of the greatest service in establishing the germ theory of disease with all the consequences of this for cardiology. And from the same coal-tar which served as a source for diagnostic stains also came curative drugs when Paul Ehrlich established the science of chemotherapy.

There are of course many other aspects of cardiology which merit discussion but time and space forbid. The growth of our knowledge of congenital defects of the heart or of the history of the foetal circulation would require separate monographs.

It is not possible to conclude however without taking note of one trend. It appears that as we probe deeper and deeper into the study of various heart disorders, notably atherosclerosis, hypertension and the problem of the failing heart, we find that more and more they involve a biochemical approach. This may be designated the biochemical phase of cardiological research—an era too recent for historical analysis.

Note

The literature on William Harvey and on the history of cardiology is already voluminous. In order to conserve space no attempt is made here to give a full bibliography. This is done the more readily since there has recently appeared an excellent reading list prepared in anticipation of the celebration of the 300th anniversary of Harvey's death in 1957. The list appears in *Current Work in the History of Medicine,* January-March, 1956, No. 9, p. 57-62.

This bibliography which appears quarterly is published by the Wellcome Historical Medical Library in London and is doubtless available for consultation in any medical library.

The Histology of the Heart and Its Changes with Age*

By
MAURICE LEV, M.D.†

(With 6 illustrations)

I AM PRESENTING the histology of the heart, from the standpoint of a pathologist. From my vantage point, I have had to delve into various histologic problems, to elucidate pathologic findings. The histology that I will present will therefore not be of the exact, minute type important to this histologist, but of the type necessary to the pathologist in evaluating pathologic findings. I will deal with: (1) the epicardium, (2) the endocardium, (3) the valves, and (4) the myocardium. I will not deal with the coronary arteries and veins. I will present these structures from the standpoint of: (1) basic histology, (2) normal variations, and (3) aging changes.

EPICARDIUM

The epicardium in the newborn consists of a core covered by a mesothelial lining. The core consists of collagenous fibers with a scant sprinkling of elastic fibers. The epicardium over the atria is thicker than that over the ventricles, and it is modified by fat accumulations in various spots, as will be described below. There is selective thickening with fibroelastic proliferation over the region of the SA node and the adjacent right atrial appendage.

By maturity, changes occur in the core, and a new layer is added beneath the mesothelial lining, consisting of dense collagenous tissue. The core now shows an increase in elastic fibers which are most dense near the new layer. With advancing age, there is a still further increase in elastic fibers. The selective fibroelastic thickening over the SA node region is now advanced.

The above basic structure is altered by a progressive accumulation of fat tissue in a distinct, grossly visible pattern. This is already present at birth, and is found in the deepest portion of the epicardium. The basic fat pattern at birth is as follows: A small fat pad is seen at the angle between the aorta, the right atrial appendage and the right ventricle. This pad may extend to the base of the pulmonary artery. Fat is also seen in the right atrioventricular groove anteriorly, and at the apex. By maturity, there is a considerable increase in fat in these regions, becoming more extensive along the coronary arteries and veins. The fat along the right atrioventricular groove increases maximally, with that of left next. With advancing age, fat appears at the entry of the pulmonary veins, the superior vena cava posteriorly, and at the entire base of the aorta. Fat likewise extends from the left circumflex upward over the left atrium, and involves the SA node region and the intercaval band. By the fifth decade, fat from all these regions may become confluent. The left ventricle in general, however has the least amount of subepicardial fat.

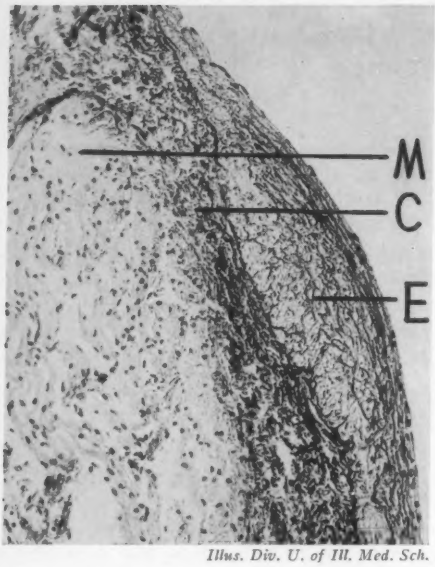
We do not know at the present time, whether the above basic structure, variations and aging changes in the epicardium are indirectly related to hemodynamic stress, emanating from within the heart, or directly from contiguous coronary arteries and veins and surrounding structures.

ENDOCARDIUM

The structure of the endocardium at birth varies from atrium to ventricle and from spot to spot in each chamber. In general, the

* Presented at the Post-Graduate Seminar on Diseases of the Heart. Held at the Armed Forces Institute of Pathology, Washington, D.C., May 14-17, 1956, and Co-sponsored by The American Heart Association, Inc.

† Pathologist and Director of the Research Laboratories, Mount Sinai Hospital, Miami Beach, Florida; Professor of Pathology, University of Miami School of Medicine, Coral Gables, Florida.



Illus. Div. U. of Ill. Med. Sch.

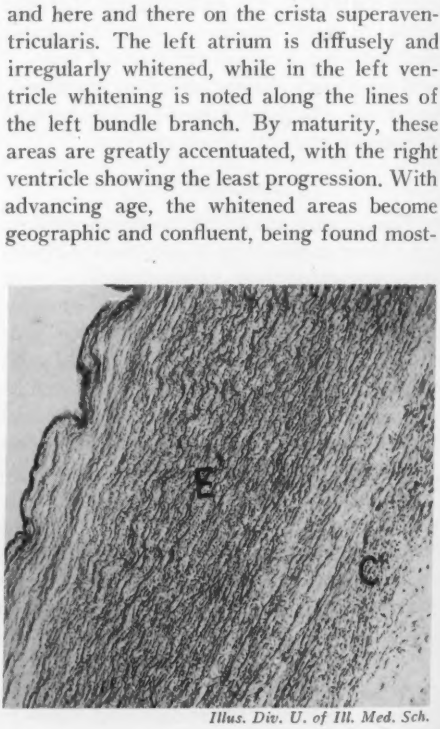
FIG. 1. Photomicrograph of the endocardium of the right atrium at birth, showing endocardial hypertrophy. Weigert-Van Gieson stain. ×132.
E—Endocardial hypertrophy;
C—Core of endocardium;
M—Myocardium.

endocardium of the atrium is thicker than that of the ventricle, and that of the left atrium is thicker than that of the right. The simplest type of endocardium consists of an endothelial lining beneath which there is a delicate elastic layer followed by a small amount of connective tissue. This type is found in areas of both ventricles. In the atria, beneath the endothelium, there is a fibroelastic core with the elastic fibers congregated towards the endothelium.

From birth on, this basic structure is altered by focal areas of proliferation of smooth muscle cells, and elastic and collagenous fibers in the lines of blood flow. This process, which occurs beneath the endothelial lining, we have called endocardial hypertrophy (Fig. 1). The distribution of these areas takes on a relatively constant pattern and is grossly recognizable.

By maturity, there is an increase in elastic and collagenous fibers in the core, as well as a considerable increase in endocardial hypertrophy (Fig. 2). Degenerative or sclerotic changes set in in these regions of hypertrophy, which will not be discussed at present. With aging, endocardial hypertrophy becomes more diffuse, but now sclerosis dominates the picture with a marked increase in collagen in areas of hypertrophy.

The above changes can be translated into the gross. At birth, in the right atrium, there are zones of whitening (endocardial hypertrophy) around the margin of the limbus, at a spot between the insertion of the eustachian valve and distal wall of the limbus, and at the base of the medial and inferior leaflets of the tricuspid valve. In the right ventricle they are noted at the base of the pulmonic valve, and here and there on the crista supraventricularis. The left atrium is diffusely and irregularly whitened, while in the left ventricle whitening is noted along the lines of the left bundle branch. By maturity, these areas are greatly accentuated, with the right ventricle showing the least progression. With advancing age, the whitened areas become geographic and confluent, being found most-



Illus. Div. U. of Ill. Med. Sch.

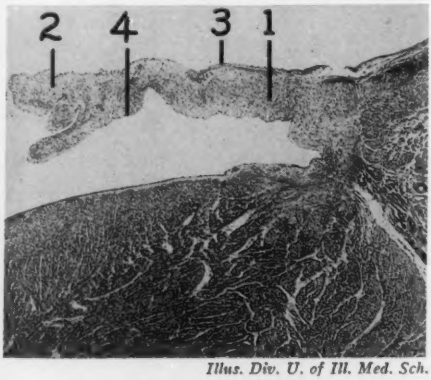
FIG. 2. Photomicrograph of the endocardium of the left atrium at 15 years of age, showing marked endocardial hypertrophy and early sclerosis. Weigert-Van Gieson stain. ×132.
E—Endocardial hypertrophy;
C—Core of endocardium.

ly in the left artium, and next in the right atrium. In the left ventricle, whitening extends down to involve the papillary muscles and the apical endocardium. The right ventricle remains relatively spared in this process.

This process of endocardial hypertrophy is similar to what we have called endophlebohypertrophy in the veins[1-3] and endarterial hypertrophy.[4] We are dealing with the reactions of the inner lining of vascular channels to hemodynamic stress.

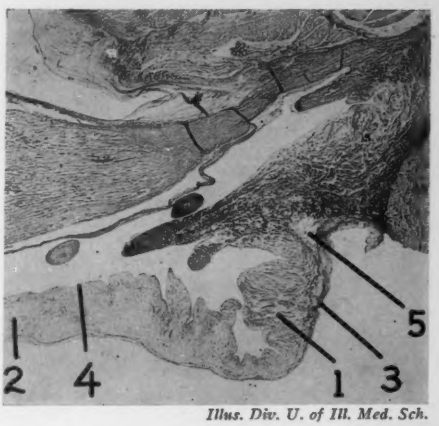
Valves

There are three parts to both the atrioventricular and semilunar valves[5]: (1) the cusp or leaflet, (2) the valve ring, and (3) the annulus. The cusp or leaflet in turn consists of a spongiosa, a fibrosa, and the endothelial coverings—a proximalis and a distalis, named atrialis and ventricularis in the atrioventricular valves, and ventricularis and arterialis in the semilunar valves. There are certain basic differences between the atrioventricular and semilunar valves: (1) the attachment of the chordae tendineae to the atrioventricular valves alters their structure in contrast to the semilunar valves, (2) the annulus of the atrioventricular valves is not as extensive as that of the semilunar valves, (3) there is a prominent ring spongiosa in the semilunar valves which is not as distinct in the atrioventricular valves.



Illus. Div. U. of Ill. Med. Sch.

Fig. 3. Photomicrograph of leaflet of mitral valve at birth. Weigert-Van Gieson stain. ×25.
1—Fibrosa; 2—Spongiosa; 3—Atrialis; 4—Ventricularis.



Illus. Div. U. of Ill. Med. Sch.

Fig. 4. Photomicrograph of leaflet of mitral valve at 15 years of age. Weigert-Van Gieson stain. ×32.
1—Fibrosa; 2—Spongiosa; 3—Atrialis; 4—Ventricularis; 5—Fat accumulation.

Atrioventricular valves. The basic structure at birth (Fig. 3) consists of a fibrosa on the ventricular side, situated most proximally, and a spongiosa on the atrial and ventricular side, situated mostly distally. The ventricularis is thin, consisting of an endothelial lining and a single elastic lamella. The atrialis is thick, consisting of an endothelial lining with a considerable zone of endocardial hypertrophy superimposed on collagenous tissue. There is little difference at birth between the mitral and tricuspid valves. By maturity (Fig. 4), there is an increase in elastic fibers in the spongiosa with disruption of the architecture and loosening of the fibrosa. There is an increased amount of endocardial hypertrophy in the atrialis and the process appears in the ventricularis. The above changes are much more marked in the mitral valve than in the tricuspid. Fat accumulates at the base of the aortic leaflet of the mitral valve very early in life. The tips of the valves and the chordae especially show marked endocardial hypertrophy. With advancing age, there is marked disruption of architecture, a loss of cellularity, and elastosis of the spongiosa and fibrosa, a loosening of

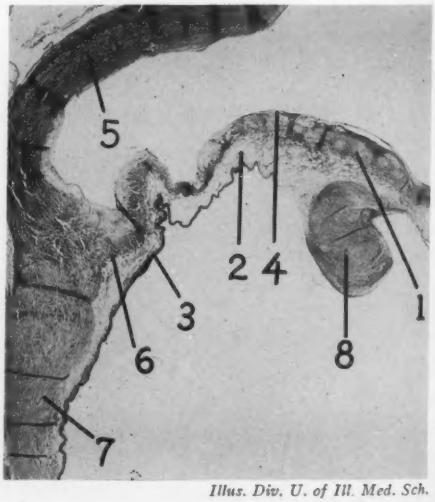
Illus. Div. U. of Ill. Med. Sch.

FIG. 5. Photomicrograph of cusp of aortic valve at birth. Weigert-Van Gieson stain. ×14.
1—Fibrosa; 2—Spongiosa; 3—Ventricularis; 4—Arterialis; 5—Aorta.

the fibrosa, and a marked increase in endocardial hypertrophy with now superimposed sclerosis of the atrialis, and less so of the ventricularis. This latter process is especially marked in the periphery of the leaflets.

Semilunar valves. The basic structure at birth (Fig. 5), consists of a core of fibrosa and spongiosa covered by ventricularis and arterialis. The fibrosa lies close to the arterialis; the spongiosa is quite extensive. The arterialis consists of an endothelial layer with no or a very delicate elastica. The ventricularis consists of internal elastic lamella with endocardial hypertrophy. At maturity (Fig. 6), the spongiosa and fibrosa show elastic fibers with some disorientation of pattern. There is an increase in endocardial hypertrophy in the ventricularis, and the arterialis acquires a distinct elastic lamella. With advancing age, sclerosis accompanies endocardial hypertrophy, with replacement by fibrous tissue. There is an increase in collagen and elastic fibers in the fibrosa and spongiosa, a disruption of architecture, and an increase in thickness of the elastica of the arterialis. The changes to maturity and old age are greatly accelerated in the aortic valve as compared to the pulmonic.

These microscopic changes in the atrioventicular and semilunar valves can be translated into the gross. The anterior leaflet of the mitral valve shows thickening of the free edge at birth, and shortly thereafter atheromas can be identified. By maturity, this leaflet presents a marked and irregular thickening. During the first two decades, the base of the aortic valve likewise begins to thicken (endocardial hypertrophy). The tricuspid and pulmonic valves show minimal changes during this period. With advancing age, the inferior leaflet of the mitral becomes involved in a focal nodularity, as the aortic leaflet becomes more severely involved. There is now also a slight thickening of the tricuspid and the base of the pulmonic valves. Simultaneously, the corpora aurantii of the aortic valve have increased in thickness with similar thickening of the lines of



Illus. Div. U. of Ill. Med. Sch.

FIG. 6. Photomicrograph of cusp of aortic valve in old age. Weigert-Van Gieson stain. ×13.
1—Fibrosa; 2—Spongiosa; 3—Ventricularis; 4—Arterialis; 5—Aorta; 6—Valve ring; 7—Annulus; 8—Corpus Arantii.

closure. In old age, there is marked thickening of the base of the aortic cusps with, in some instances, agglutination of the commissures and the production of Lamblian excrescences. Likewise, severely involved is the mitral valve, less so the tricuspid valve, and least the pulmonic valve. The latter may show a slight thickening of the base and of the noduli Morgagni.

It is thus evident that the valves are greatly affected by hemodynamic stress as is the endocardium.

Myocardium

There is a difference in the structure and in the aging changes of the atrial and ventricular myocardium. The atrial myocardium is more loosely arranged with a greater amount of connective tissue. Thus the reticular nets, or the basement membranes of the myocardial fibers, show a somewhat different pattern in the atria than in the ventricles. At birth, however, they are of similar thickness. By maturity, elastic fibers become very abundant in the atria, but are scarce in the ventricles. The reticular basement membranes, however, become thicker in the ventricles than in the atria. There is an increase in collagenous tissue in both atria and ventricles, but it remains more marked in the atria. With advancing age, the reticular network in the ventricles becomes very prominent. There is only a slight increase in elastic and collagenous fibers in the ventricles in old age.

There are no true anatomic cleavage planes between isolated muscles in the ventricular myocardium. The ventricular myocardium consists of one muscle mass divided and subdivided into branching and intercommunicating fasciculi. However, the direction of the fasciculi in any one plane is more or less constant, giving the ventricular myocardium a distinct architecture, the epicardial fibers being more or less at right angles to the endocardial fibers at any one point. Thus it is not wise to use the nomeclature sinuspiral and bulbospiral muscles.[6]

Summary

The above discussion of the histology of the heart does not enter into many details important to the histologist. An attempt, however, has been made to present the histology from the hemodynamic standpoint, and as related to advancing age, to yield a baseline for the pathologist. A more complete discussion of the gross and microscopic aging changes in the heart will be forthcoming at a later date.[7]

References

[1] Lev, M., and Saphir, O.: Endophlebohypertrophy and phlebosclerosis. I. The popliteal vein. A. M. A. Arch. Path., 51:154, 1951.

[2] Lev, M., and Saphir, O.: Endophlebohypertrophy and phlebosclerosis. II. The external and common iliac veins. Am. J. Path., 28:401, 1952.

[3] Littman, M. C., Lev, M., and Saphir, O.: Endophlebohypertrophy and phlebosclerosis. III. The left innominate vein and superior vena cava. Angiology, 4:301, 1953.

[4] Lev, M., and Sullivan, C. M.: The relationship of aging changes to the development of arteriosclerosis in the human aorta. J. Geront., 6:118, 1951.

[5] Gross, L., and Kugel, M. A.: Topographic anatomy and histology of the valves in the human heart. Am. J. Path., 7:445, 1931.

[6] Lev, M., and Simkins, C. S.: Architecture of the human ventricular myocardium. Technic for study using a modification of the Mall-MacCallum method. Lab. Invest., 5:396, 1956.

[7] Lev, M., and McMillan, J. B.: The aging heart. To be published.

The Conduction System in the Human Heart*

By
MAURICE LEV, M.D.†

(With 6 illustrations)

I WISH to discuss certain structures which are considered to be the conduction system of the heart. I will not deal with the controversial question as to whether these structures are in effect the conduction system. The structures that I will discuss are the SA node, the AV node and bundle, the right and left bundle branches, the Purkinje fibers, Mahaim's paraspecific fibers and the fibers of Kent. I will deal with these structures from the viewpoint of gross anatomy, microscopic architecture, methods of study and aging changes.

SINOATRIAL NODE

This structure lies in the sulcus terminalis between the superior vena cava and the right atrial appendage. It extends from the recess of the right atrial appendage to Wenckebach's bundle, and lies on the lateral aspect of the posterior crest. It is difficult to dissect grossly because of the great amount of collagenous and elastic tissue it contains. It thus blends with the surrounding tissue and is difficult to recognize grossly.[1]

Microscopically, however, the structure is easily recognized (Fig. 1). It consists of a plexiform network of slender muscle fibers. These are slenderer than the atrial fibers in all age groups and the nuclei are of slightly smaller diameter. The fibers possess a relatively scant number of myofibrils, with cross striations which are less prominent than those of the atrial musculature. No intercolated discs are in evidence. These muscle fibers lie in a sea of collagenous and elastic fibers which in all age groups are more copious than those of the atrial myocardium (Fig. 2). The reticular pattern consists of a fine mesh of lightly stained fibers which in all age groups is in contrast to the coarser network of more darkly stained reticular fibers enveloping the atrial myocardium. Nerve elements are in evidence in the periphery and in the midst of the superior portion. The nodal muscle fibers make connection with the musculature of the superior vena cava, the confluence of the right anterior crest and the interatrial band, the intercaval band, and the right atrial appendage. These connections occur without the intervention of Purkinje fibers.

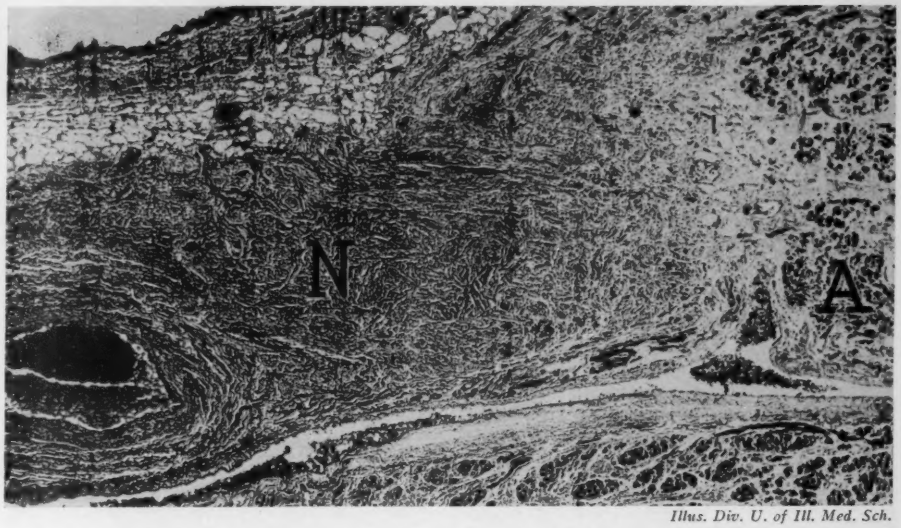
With advancing age,[2] the node grows more slowly than the remainder of the atrial myocardium. There is a progressive increase in elastic and collagenous fibers, an accentuation of the reticular network and an infiltration of fat.

The above details indicate that the SA node presents certain histologic characteristics which differentiate it from the atrial musculature. Of course, this does not necessarily imply physiologic specificity.

Utilizing our knowledge of the anatomic location of the node, the following method of sectioning and studying the node may be adopted:[1] The block of tissue for sectioning is fashioned as follows: Cut 1 is made through the atrial musculature at right angles to the sulcus terminalis in the region where the posterior crest flattens out, up to the right lateral margin. Cut 2 extends from the end of Cut 1 through the right lateral margin through the superior vena cava. Cut 3 extends through the right atrial appendage over its summit through the superior wall of the right atrium for a distance of ¼-½". Cut 4 is made from the end of Cut 3 parallel

* Presented at the Post-Graduate Seminar on Diseases of the Heart. Held at the Armed Forces Institute of Pathology, Washington, D.C., May 14-17, 1956, and Co-sponsored by The American Heart Association, Inc.

† Pathologist and Director of the Research Laboratories, Mount Sinai Hospital, Miami Beach, Florida; Professor of Pathology University of Miami School of Medicine, Coral Gables, Florida.



Illus. Div. U. of Ill. Med. Sch.

FIG. 1. Photomicrograph of sinoatrial node. Transverse section. Hematoxylin-eosin stain. ×57.
N—Sinoatrial node;
A—Atrial musculature.

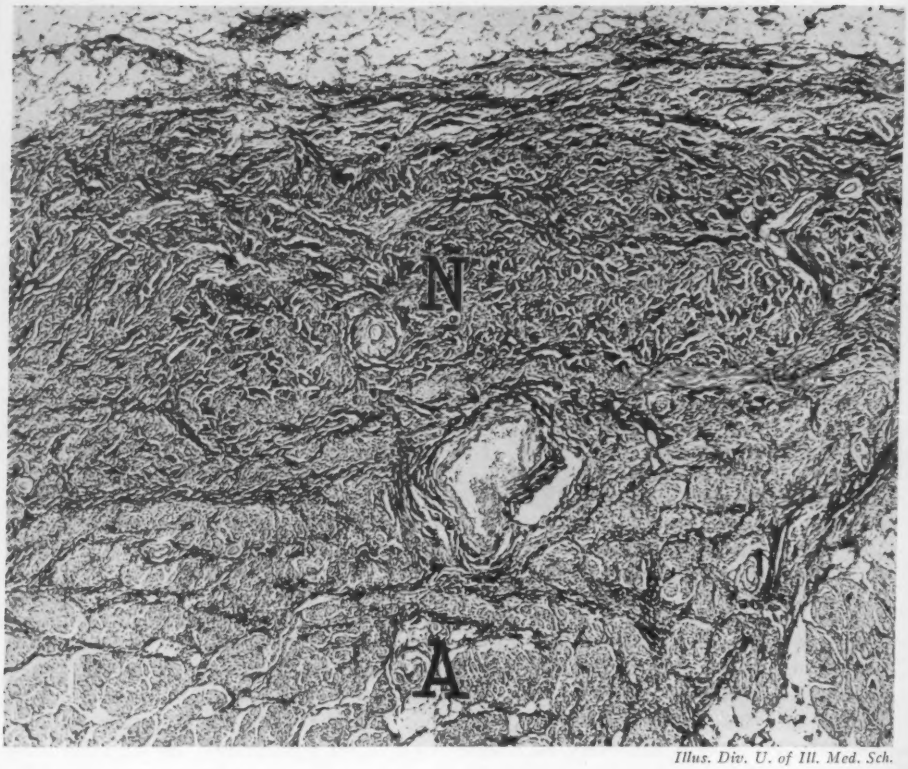
to the summit of the right atrial appendage through the superior vena cava. The block so obtained is embedded in paraffin with the posterior crest facing the microtome knife. Serial sections are cut and every 80th section is retained for a total of six sections in the beginning of the block. Thereafter every 20th section is retained through the remainder of the block. Sections are alternately stained with hematoxylin and eosin and Weigert's elastic tissue stain counterstained with Van Gieson stain.

ATRIOVENTRICULAR NODE AND BUNDLE, AND THE RIGHT AND LEFT BUNDLE BRANCHES

In contrast to the SA node, the AV node and bundle are easily dissected in the following manner (Fig. 3)[3]: the chordae tendineae of the medial part of the anterior tricuspid leaflet and of the medial leaflet are cut away and those portions of leaflet detached at their ring base and from the pars membranacea and central fibrous body. The atrial endocardium is removed from the region bounded by the eustachian valve, the coronary sinus and the denuded valve ring attachment. This reveals a thin sheet of atrial muscle coursing obliquely or at right angles to the base of the tricuspid valve. After cutting this layer, the AV node becomes evident. The ramus septi fibrosi can be traced from its origin from the right (and occasionally the left) coronary artery into the midst of the node. The right layer of the posterior aspect of the pars membranacea is now removed. This reveals the branching portion of the AV bundle. The posterior end of this bundle is followed into the central fibrous body, the right aspect of which is removed with a sharp scalpel. Continuity between the AV node and bundle is thus established.

The AV bundle is then traced into the right branch at the distal angle of the pars membranacea. This branch follows a course along the inferior aspect of the septal band of the crista supraventricularis between the conus and the sinus of the right ventricle. Its first portion is usually subendocardial or relatively superficial up to the level of the muscle of Lancisi. It then dips into the myocardium, becoming superficial only at its distal third, where it terminates at the moderator band.

The beginning of the left bundle branch



Illus. Div. U. of Ill. Med. Sch.

FIG. 2. Photomicrograph of sinoatrial node. Transverse section. Weigert-Van Gieson stain. ×57.
N—Sinoatrial node;
A—Atrial musculature.

can be dissected with difficulty in the following manner: the pars membranacea and all tissue anterior to it are removed so that one sees both sides of the septum from the vantage point of the AV bundle; the endocardium is then painstakingly separated from the left aspect of the ventricular septum revealing the fasciculi of the left branch. One can follow these fasciculi only for a short distance downward.

Histologically, all of the above structures are easily identified by their position and the following general characteristics:[4] (a) sheath, (b) cytoplasm of the cells and (c) elastic network. In addition, some parts have further differentiating characteristics.

(a) Sheath. All parts contain endothelial lined structures which surround and interdigitate between the fasciculi. This gives all structures an increased cellularity which is most marked in the AV node and bundle. From the end of the node to a considerable distance down the bundle branches, the sheath surrounds a distinct loculated space.

(b) Cytoplasm of cells. The cytoplasm of the muscle cells of all parts is less eosinophilic due to a lesser number of myofibrils in comparison to the ventricular myocardium. The myofibrils are cross-striated in the adult.

(c) Elastic network. At any age level, all structures show an increase in elastic fibers as compared with the musculature of the atria and ventricles.

In addition, each structure has certain individual characteristics:

(1) AV node. (Fig. 4). This lies adjacent

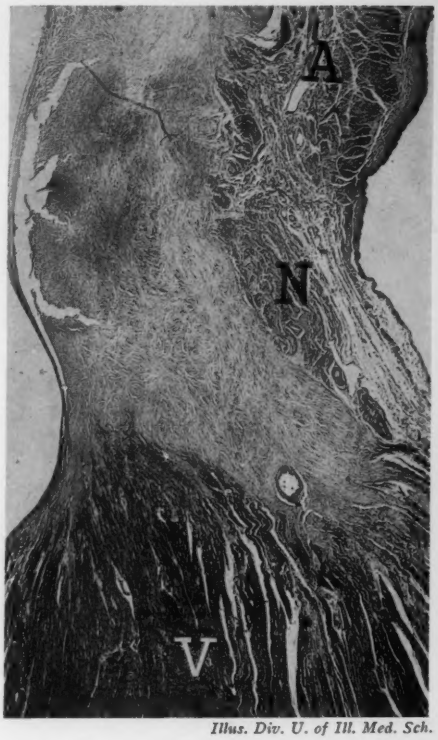
to the central fibrous body above the base of the septal leaflet of the tricuspid valve in the posterodistal part of the atrial septum. It consists of a loose network of small fibers which are smaller than the atrial and ventricular fibers.

(2) AV bundle (Fig. 5). This consists of two parts: (a) the penetrating portion passing through the central fibrous body, and (b) the branching portion in the lower part of the pars membranacea above the muscular ventricular septum. The latter part may, however, lie on the left side of the septum, and uncommonly on the right. Its fibers are likewise smaller than those of the atria and ventricles.

(3) Left bundle branch (Fig. 6). The fibers lie beneath the endocardium and are divided into anterior and posterior radiations. The fibers become progressively larger as they proceed apexward. Their basement membranes are more prominent than those of the myocardium. The terminal fibers (Purkinje cells) end in the myocardium of the anterior and posterior papillary muscles and also proceed to the apex. Their exact manner of termination is controversial.

Illus. Div. U. of Ill. Med. Sch.

FIG. 3. Dissection of the AV node, bundle, and right bundle branch.
1—Atrioventricular node; 2—Penetrating portion of AV bundle; 3—Branching portion of AV bundle; 4—Right bundle branch.



Illus. Div. U. of Ill. Med. Sch.

FIG. 4. Photomicrograph of AV node. Oblique section. Hematoxylin-eosin stain. ×20.
A—Atrial musculature;
N—AV node;
V—Ventricular musculature.

(4) Right bundle branch (Fig. 6). Its first portion is subendocardial, and its fibers are smaller or equal to those of the adjacent myocardium. The second portion is intramyocardial and mimics the myocardial fibers. The third portion is again subendocardial and its fibers are larger and begin to resemble Purkinje cells. These cells terminate in the region of the anterolateral papillary muscle. The exact manner of their termination is controversial. It is not definitely known whether Purkinje fibers are present in the myocardial wall. In addition to the standard topography there are variations in the structure of the right bundle branch. Thus occasionally two right branches are given off, with one ending blindly, or a single

Illus. Div. U. of Ill. Med. Sch.

FIG. 5. Photomicrograph of the AV bundle (Bundle of His). Transverse section. Hematoxylin-eosin stain. ×20.

A—Atrial musculature;
B—AV bundle;
V—Ventricular musculature.

branch may bifurcate and then the two components rejoin to form one.

With advancing age[5] there is an increase in collagenous tissue, an increase in elastic tissue, an infiltration of fat and an increase in density of the reticulum.

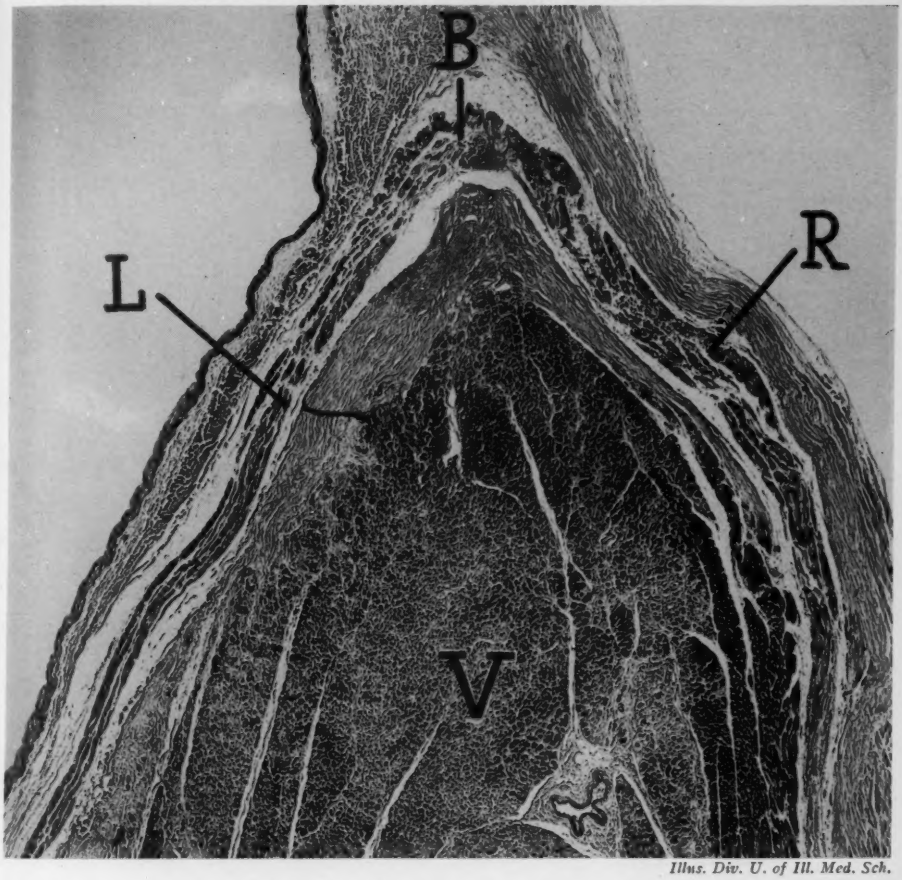
The above anatomic facts make possible a method of cutting which we have devised, as follows:[4] The parietal and inferior walls of both atria and ventricles are cut away leaving the septal walls. The pars membranacea is observed carefully, as well as the eustachian valve, the coronary sinus, the central fibrous body, the muscle of Lancisi and the crista supraventricularis. This gives the general location and direction of the AV node, bundle and right branch. The baseline for cutting, Cut 1, is made along a line ¼-½″ below the moderator band to produce an angle of about 45° with the line of the crista. Cut 2 is made at right angles to Cut 1 and passes through the junction of the eustachian valve and the limbus. Cut 3 is made at right angles to the second cut, passing through the base of the aorta. Cut 4 is made just lateral to the moderator band at right angles to the third cut. This leaves a rectangle of muscle containing all of the desired structures with the exception of the lower aspect of the left bundle branch fasciculi. Cut 5 is made at right angles to the baseline passing through the middle of the pars membranacea. This yields block 1. Cut 6 is made at right angles to the baseline passing through the muscle of Lancisi. This yields block 2. Cut 7 is made at right angles to the baseline dividing the remainder of the tissue into blocks 3 and 4. Every 20th section is saved through block 1, and every 40th section thereafter. These sections are stained with hematoxylin-eosin and elastic Van Gieson stains.

We are now working on a much more inclusive method of studying the conduction system, which includes not only the above structures but the connections between the SA and AV nodes and the peripheral fasciculi of the left bundle branch.[6]

The above discussion reveals again, as in the case of the SA node, that we are dealing with structures which have certain differentiating characteristics and hence possess histologic specificity. As to whether this also means functional specificity is a controversial question.

MAHAIM'S PARASPECIFIC FIBERS

Mahaim and his associates[7-9] have shown that there are small muscular communications between the AV node, bundle and the beginning of the left bundle branch and the ventricular myocardium. In man, there is no such communication between the right bundle branch and the septum. We have found these communications to be more common before and at birth, than in later life. We have also found little twigs given off from the right branch, which enter the septum but end blindly without joining the ventricular myocardium. The function of Mahaim's fibers is today a controversial question.



Illus. Div. U. of Ill. Med. Sch.

FIG. 6. Photomicrograph of AV bundle bifurcating into right branch and some fasciculi of the left branch. Transverse section.
B—AV bundle; R—Right branch;
L—Some fasciculi of left branch;
V—Ventricular musculature.

KENT'S FIBERS[11-16]

As is well known, Kent had found communications between atria and ventricles in addition to the AV bundle, and hence postulated that heart conduction proceeded along multiple pathways. This was followed by a tremendous literature affirming or denying the presence of these extra communications. In a recent study of 22 fetal and newborn hearts, we found no muscular communications between the atria and ventricles outside the AV bundle.[10]

SUMMARY

It therefore becomes evident that certain structures are present in the heart which have a histologic specificity which may constitute a conduction system. Time does not permit the discussion of the nerve supply to these structures and to the atrial and ventricular myocardium, which may be related to the theory of conduction.

REFERENCES

[1] Lev, M., and Watne, A. L.: Method for routine

histopathologic study of human sinoatrial node. A. M. A. Arch. Path., 57:168, 1954.

[2] Lev, M.: Aging changes in the human sinoatrial node. J. Geront., 9:1, 1954.

[3] Widran, J., and Lev, M.: The dissection of the atrioventricular node, bundle and bundle branches in the human heart. Circulation, 4:863, 1951.

[4] Lev, M., Widran, J., and Erickson, E. E.: A method for the histopathologic study of the atrioventricular node, bundle and branches. A. M. A. Arch. Path., 52:73, 1951.

[5] Erickson, E. E., and Lev, M.: Aging changes in the human atrioventricular node, bundle and bundle branches. J. Geront., 7:1, 1952.

[6] Lev, M., and McMillan, J. B.: A semi-quantitative method for studying the entire heart for electrocardiographic correlation. To be published.

[7] Mahaim, I., and Benatt, A.: Nouvelles recherches sur les connexions supérieures de la branche gauche du faisceau de His-Tawara avec la cloison interventriculaire. Cardiologia, 1:61, 1938.

[8] Mahaim, I., and Winston, M. R.: Recherches d'anatomie comparée et de pathologie expérimentale sur les connexions hautes du faisceau de His-Tawara. Cardiologia, 5:189, 1941.

[9] Mahaim, I.: Kent's fibers and the AV paraspecific conduction through the upper connections of the bundle of His-Tawara. Am. Heart J., 33:651, 1947.

[10] Lev, M., and Lerner, R.: The theory of Kent. A histologic study of the normal atrioventricular communications of the human heart. Circulation, 12:176, 1955.

[11] Kent, A. F. S.: Researches on the structure and function of the mammalian heart. J. Physiol., 14: 233, 1893.

[12] Kent, A. F. S.: Observations on the auriculoventricular junction of the mammalian heart. Quart. J. Exper. Physiol., 7:192, 1913.

[13] Kent, A. F. S.: The right lateral auriculoventricular junction of the heart. J. Physiol., 48:XXII, 1914, Proc. Physiol. Soc. (March 14), 1914.

[14] Kent, A. F. S.: Illustrations of the right lateral auriculoventricular junction in the heart. J. Physiol. 48:LXIII, 1914, Proc. Physiol. Soc. (June 27), 1914.

[15] Kent, A. F. S.: A conducting path between the right auricle and the external wall of the right ventricle in the heart of the mammal. J. Physiol., 48: LVII, 1914, Proc. Physiol. Soc. (June 27), 1914.

[16] Kent, A. F. S.: Neuromuscular structures in the heart. Proc. Roy. Soc. London, s. B. 87:198, 1913-14.

The Anesthetic Management of the Patient with Heart Disease*

By

MAJOR TIMOTHY G. BARILA, MC, *U. S. Army*†

"THE IDEAL ANESTHETIC"

THE qualities desired in an ideal anesthetic have been well summarized over the years, and are particularly pertinent for the patient with heart disease. The ideal anesthetic must meet the requirements of at least four individuals: the patient, the surgeon, the anesthesiologist and the internist. The patient desires not only rapid and pleasant induction with an anesthetic which is nonirritating and free from unpleasant odor, but also a recovery period which is free of discomfort. The surgeon desires an agent which produces complete muscular relaxation and does not increase capillary bleeding. The anesthesiologist desires an anesthetic to have a wide margin of safety, to be excreted from the body rapidly and unaltered, to cause a minimum of functional or organic injury during and following its use, to be sufficiently potent so that a high percentage of oxygen may be employed in the inhaled mixture at all times, and to diffuse sufficiently rapidly to allow moment-to-moment control of depth of anesthesia. The internist, who has determined the optimal time of operation following treatment with bed rest, various diuretics, digitalis compounds, vasodilating drugs, and fluid and salt control, desires his patient to be returned to him in a reasonably similar condition of equilibration.

No known anesthetic agent fulfills all the qualifications listed, nor should one expect one to do so, since the capabilities of the anesthesiologist and his familiarity with agents, technics and the individual requirements of the surgeon are more important factors than the mere use of a theoretically safe or "ideal" agent.

TEAMWORK

The care of the cardiac patient obviously requires teamwork among the entire staff involved in patient care—teamwork in the true sense of the word, not just a request for another specialist to aid in evaluating the patient, but teamwork such as that mobilized at Mayo Clinic, for example. There, a large group of skilled, interested medical and paramedical people have been able to utilize successfully the Gibbon pump for heart-lung bypass with the surgical cure of some types of heart disease previously amenable only to palliative procedures; i.e., the freeing of the pulmonary outflow tract with closure of the interventricular septal defect in contrast to a Blalock or Potts-type bypass procedure in the management of tetralogy of Fallot. Such teamwork implies the fuller utilization of the anesthesiologist in the medical-surgical team.

The daily operating room schedule is completed, for the most part, by 2 P.M. Thus, several physicians are available each day for duty other than in the operating section. Considerable time is spent by the anesthesiologists in the preoperative evaluation of patients and for the postoperative follow-up. This service has been appreciated by internist and surgeon alike and should lead to better overall care of patients. One or more staff anesthesiologists are freely available in the hospital not only during the hours of scheduled surgery but during the entire twenty-four hours of each day, every day of the year. We have felt that this is necessary since, in any busy hospital, acute and critical problems requiring immediate attention may

* Presented at the Post Graduate Seminar on Diseases of the Heart, Armed Forces Institute of Pathology, Washington, D.C., May 14-17, 1956.

† Chief, Dept. of Experimental Surgery, Walter Reed Army Institute of Research, WRAMC. Present address: Chief, Anesthesia and Operating Room Service (8059), Tokyo Army Hospital, APO 500.

arise at any time in the obstetrical division, the operating theater, the emergency room or on medical floors. For example, a newborn baby in need of immediate resuscitation cannot await the arrival of a physician who is on call twenty minutes away from the hospital nor can the small child in the emergency room survive very long with a piece of orange pulp incarcerated in the larynx. In this day of rapid travel with the automobile and airplane we are frequently called upon to assist in the emergency room with surgeons, orthopedists or neurosurgeons in the treatment of shock, hemorrhage and multiple wounds for two or more patients who arrive simultaneously. This is one place where the team has a real service to offer. The anesthesiologist assists in the treatment of shock, and the administration of fluid and blood, or blood substitutes. He is interested in establishing an adequate airway in the patient with multiple facial and cheek injuries or he may assist the neurosurgeon in emergency tracheotomy as an immediate lifesaving procedure for wounds about the head.

Psychological Aspects

But apart from the emergency aspects, the anesthesiologist plays a real role in the psychological aspects of patient management. This factor should occupy a prominent part in our considerations of the management of the patient with heart disease. Anesthesiologists see too many patients who, convinced they would die because of surgery and anesthesia, have failed to survive a procedure, even of an almost minor nature.

A healthy young warrant officer was told he had subacute appendicitis which should be surgically corrected for his ultimate benefit, but this man was convinced his affliction was extremely serious and life-threatening. Two postponements of his appendectomy due to urgency of the surgical schedule further corroborated his views and he became convinced he would not survive his operation. Somewhat to his surprise, no doubt, he had an easy time of the surgery and early post operative period, but no one had time to discuss fully with him just what had been done. Consequently, as the time approached for removal of his sutures, he became more and more apprehensive, and to shorten the story, when the surgeon arrived on the day the sutures were due to be removed, the patient was found dead. The Pathology Department found no emboli or other cause for this death.

Conversely, some of the surgical successes attributed to the skillful surgeon, aided by a superbly managed anesthetic, have been due, in great part, to an unquenchable desire to survive on the part of the patient.

Many patients have more concern over the anesthesia which is to be "inflicted" upon them than they are regarding their illness. The anesthesiologist, as a doctor, can spend time with such a patient and "talk out" many of his fears, or even "sell" him on the adequacy and benign nature of current anesthetic management. In addition, the anesthesiologist gains valuable information in this informal interview, such as previous anesthetic experiences and complications, sensitivities to drugs, and the ability to calculate the proper premedication which will aid in avoiding the possibilities of a sudden demand on the heart during crucial induction of anesthetic. He determines, also, the maintenance drugs the patient is using.

Iatrogenic Complications

Modern pharmacology has become a two-edged sword to the anesthesiologist. Previously, he was interested, at most, in insulin and thyroid medication, but with the wide use of potent hormones and tranquilizing drugs which are of marked benefit to the patient, he is faced with the possibility of profound vasodepression when synergistic anesthetic agents are added to these maintenance drugs. The nature of anesthetic agents themselves seems on the threshold of new horizons, as we approach true analgesics, which completely relieve pain without respiratory or circulatory depression. Experiences in Korea, in World War II, and in

geriatric patients have aided us greatly in formulating the management of patients with acute or chronic heart disease. These patients are inordinately susceptible to all depressant drugs. Injudicious use of opiates, when pain is not present, penalizes the patient. Motion or position change in the patient with a labile vascular system can precipitate collapse.

Preoperative Evaluation

In evaluating the patient preoperatively, the greatest factor or measurement is probably the status of the circulating blood volume. Since World War II an appreciation of hypervolemia and increased red cell mass has resulted from blood volume studies. It appears now to be just as important to recognize and treat patients with excesses as formerly when deficits were found. The National Research Council has pointed out that in humans, starvation can proceed to the point of wasting of one quarter of the body weight before circulating blood shows any change in percentage relationship of red cells or proteins. Blood volume determination, however, on the individual who has been starved, will show marked deficits in total values for both red cells and plasma proteins. Restoration to normal is essential for this patient if surgical procedures or anesthesia are to be successful and safe. I am sure many other examples can come to mind. Similarly, patients with hematocrit values above 50 present a picture of polycythemia which is detrimental. For example, a fifty year old male patient who, scheduled for surgical removal of a renal tumor, was found to be grossly overweight, somewhat hypertensive, had dyspnea on exertion and the hematocrit was 56%. This patient while at rest or doing light work was already calling upon his reserves to carry on normal functions of circulation and respiration. If the stress or strains of general anesthesia and operative procedure had been added to this patient's burden, failure of vital systems would occur. With an excess of red cells present, the viscosity of the blood is increased and the work of the heart in maintaining an adequate output for normal circulation is also increased. If relative viscosity of blood is too high or if cardiac reserve is low or if hypoxia occurs as a result of difficulties during anesthesia, then a critical point may be reached beyond which the heart is able to cope with the load. Circulation is retarded and hypoxia becomes severe following which changes occur in permeability of endothelium which may finally lead to intravascular coagulation or thrombosis. At the same time, the heart may begin to fail and pulmonary edema during anesthesia may become evident. The clinical evidence of increased viscosity is the appearance of a cape-like area of cyanosis involving the head, neck, shoulders and even the dependent parts of the body. This "cape" occurs with sufficient regularity in the induction of anesthesia that it has been an extremely important prognostic sign to us, warning of the probability of more serious problems if the patient is not ideally managed during the rest of the procedure. The cyanosis frequently does not disappear even when oxygen is administered in adequate volume and under a pressure which will guarantee normal ventilation. Thus, we feel that a patient with a hematocrit over 50 is not suitable subject for general anesthesia.

This problem is compounded in the patient in whom polycythemia is necessary for life, such a cyanotic heart disease, who is scheduled for surgical correction of his disease. All his compensatory efforts become detrimental after the septal defect is closed and the tremendous blood volume begins to course through the subdeveloped ventricle which begins to fail. Less than full replacement of blood loss during surgery, or phlebotomy, has helped tide these patients over this period.

Shock Therapy

In selected cases of progressive shock, with blood vessels no longer able to react to humoral stimulation, the administration of adrenal cortical hormones may lead to res-

toration of proper hemodynamics. In this restoring of vascular responsiveness lies the best possible use of intravenous hydrocortisone in massive dosage. However, one should bear in mind that these agents do not and should not be used to replace the standard methods to combat shock, including the administration of blood and vasoconstrictors. Indeed, these agents may not exhibit their beneficial effects until such measures have been employed.

Several examples of the immediate, dramatic, beneficial and life-saving effects brought about by these agents come to mind, even in patients who appeared to be in what is erroneously called "irreversible shock" for hours or even days following extensive surgery.

The use of vasodilator agents, or, to say it in another way, the decrease in peripheral resistance by drugs, with the concomitant easing of the cardiac work, has already been mentioned. Its rationale is clear in that tissue perfusion continues adequate in the face of the resultant low pressure because of increased flow of blood at the cellular level, but at present the use of such potent vasodilators in the face of extreme shock requires a great deal of courage on the part of the physician. There have been sufficient good results in such patients when such a regimen has been attempted, after conventional methods had failed, to warrant further evaluation.

Optimal Time for Surgery

The evaluation of the patient regarding the optimal time for surgery is difficult, especially in patients with cardiac disease. Harkin in the "New England Journal of Medicine," has pointed out the grave responsibility for all physicians who see patients with mitral stenosis. In his series, the surgical mortality rate for patients with Grade 3 mitral stenosis has progressively fallen to 0.5% while that for Grade 4 patients has remained relatively stable at 16%. Delaying surgery on a patient until he becomes a Class 4, therefore, decreases his chances of survival over 30-fold.

Proper preoperative evaluation has avoided the "night before" admissions with their occasional fatalities due to inadequate workup or treatment. This increase in patient safety, and decrease in discomfort and mortality is again the result of teamwork.

In general, patients with heart disease tolerate a surgical procedure quite well. Exceptions are those with conditions known to cause most of the operative and immediate postoperative deaths such as severe congestive failure, recent myocardial infarction, angina decubitus and Stokes-Adams syncope. In such situations one must seriously consider whether operation can be tolerated at all and, if so, whether the patient is likely to survive the cardiac condition long enough to enjoy the benefits accruing from operation.

Unfortunately there are no specific tests of cardiac reserve as we in anesthesia see it; that is, a test or tests which simulate the burden of operation with its associated apprehension, effects of toxic anesthetic agents, retraction, handling of viscera, blood loss and replacement, disturbed respiratory function and the many other unnatural factors which accompany major surgery. Nevertheless, aside from those cardiac patients in whom immediate operation is imperative and holds some promise of worthwhile results, evaluation and improvement of heart function before operation will often pay dividends.

The history is important, particular attention being paid to substernal pain, dyspnea and edema. Cardiac pain becoming more severe, more frequent or occurring with lesser stress suggests existing or impending myocardial infarction. It also infers that any excessive preoperative apprehension, struggling during induction, anoxia or hypotension may have serious consequences. Corroborative electrocardiographic changes of recent myocardial infarction precludes most operations until evidence of healing occurs.

Exertional dyspnea, edema or other symptoms suggesting congestive failure should be investigated and energetically treated prior to operation in most instances. Digitalization, restriction of sodium and the use of a diuretic are usually indicated. Unless time is a factor, slow digitalization is desirable but rapid therapy by parenteral routes is often necessary in surgical patients.

Regarding arrhythmias, the condition of the myocardium is the chief factor in evaluating surgical risk. Auricular fibrillation and flutter, extrasystoles and paroxysmal tachycardia do not in themselves contraindicate an operation so long as the rate is controlled and evidence of myocardial damage does not exist. A history of ventricular tachycardia or existing heart block and coupled rhythms signify more severe grades of heart disease and increased risk.

Hypertension itself is rarely a contraindication to operation provided marked and precipitous drops in pressure are avoided. However, when associated with cardiac enlargement or congestive failure, appropriate therapeutic measures are indicated before major surgery is attempted.

The Surgical Period

Freedom from worry and apprehension before and after operation are especially important in the cardiac patient. Assurance that modern preoperative, anesthetic and surgical methods render him just as suitable to withstand operation as the normal person often imparts necessary confidence and establishes valuable rapport between doctor and patient. Discreet sedation which will dull the senses without producing depression or confusion is ideal, although often hard to obtain, and may necessitate the trial of more than one drug. Checking the degree of sedation a few minutes prior to transfer of the patient from his room to the operating suite is important. Alertness and apprehension at this time calls for administration of additional medication intravenously in many instances.

The anesthetic induction period is particularly critical in cardiac patients. Epinephrine secretion is apt to be maximum at this time and is probably a factor in initiation of some arrhythmias, and possibly accounts for some cardiac arrests. It is essential to accomplish smooth induction without excitement, struggling, straining, breath-holding or other causes of associated hypoxia. Irregularities developing at this time, such as occasional premature beats, are generally not significant. However there are certain instances where gross irregularities serve as definite warning signals.

The majority of anesthetic deaths are no doubt due to inadequate pulmonary ventilation. A patent airway is essential. This is especially true in the cardiac patient. The effort expended in ventilating himself should be kept at a minimum. Likewise, he will do best with an anesthetic agent which admits high concentrations of oxygen. The orthopneic patient is preferably kept in his most comfortable position when moved to the operating table. Any position which decreases vital capacity or has deleterious effects on circulation, such as steep Trendelenburg, exaggerated lithotomy or jack-knife prone, should be avoided. Extensive packing which interferes with diaphragmatic function is undesirable.

All of these compromised ventilatory situations require compensation by increased positive pressure respirations which may so interfere with volume return as to cause serious hypotension. This fall in blood-pressure, or any, should be prevented. Hypotension, with decreased circulation through the coronary system, is poorly tolerated. For this reason anesthetic agents should be chosen which will favor maintenance of relatively normal pressure. Shock must be prevented. Here we come to a vexing problem in the cardiac patient—the administration of parenteral fluids without overloading the circulation. Intravenous infusions should be given slowly, especially if a correction procedure has been accomplished which has changed the body's hemodynamic flow pattern, so as to place increased work on previ-

ously little used parts of the cardiovascular system.

Continuing Management in the Post-Operative Period

Postoperatively, the anesthetic care continues in the recovery room or ward. This type of centralization of care has undoubtedly contributed markedly to the overall reduction in operation mortality in this country. Again, the major effort is toward the prevention of hypoxia.

Therapy to prevent lung complications and its resultant hypoxia consists of:

1. Stir-up Regimen. This includes: (a) turning the patient from side to side every hour; (b) having the patient take 5 to 10 deep breaths when awake every hour for the first 48 hours; (c) urging him to cough to remove mucus secretions from the lung and, if necessary, having him sit on the edge of the bed and making him cough as he is pounded gently on the back to loosen plugs; and (d) early ambulation.

2. Intercostal Blocks. These are of particular value if the patient refuses to cough because of pain following upper abdominal operations. More often than not, once the pain is relieved these patients will be most cooperative in carrying out the "stir-up regimen."

3. Tracheal Suction. If the patient refuses to cough even after an intercostal block then he may be made to cough by passing a urethral catheter through the nose into the trachea. Just sucking out the pharynx is of little help in these cases and is usually what may be expected if the task is left to a nurse, rather than to a physician, with this technique.

4. Bronchoscopy. If, in spite of the above therapy, the patient develops atelectasis or regurgitates fluid from his stomach into his trachea and cannot expel it because he is too weak, then bronchoscopy must be done.

The extreme susceptibility of many of these patients to depressant drugs has been discussed. Pain as a symptom must be carefully differentiated from the restlessness of insidious hypoxia.

Fluid and electrolyte management in surgical patients is a study of body water and ion movement in relation to trauma. Intracellular and extracellular locations of body water are profoundly influenced by pre-existing dehydration at the time of operation by intestinal tract dysfunction and by losses of extrarenal water and ions after surgery and anesthesia.

On the recovery ward we are concerned with: (1) body water; (2) renal function; (3) circulating blood volume; (4) ions of sodium, potassium, and chloride; (5) calories; (6) protein; (7) effects of trauma; and (8) mechanics of parenteral fluid administration.

The estimation of renal function before a surgical operation pays dividends on the recovery ward. A 24-hour period of observation will suffice for this purpose. Evidences of renal abnormality are: (a) failure to excrete 500 cc. of urine for 24 hours after an intake of 1000 cc. or more; (b) specific gravity of less than 1.010 in all urine specimens; (c) cellular elements or casts in the urinary sediment; (d) proteinuria; and (e) elevated blood urea nitrogen.

Other areas of teamwork between anesthesiologists and the obstetrician, the pediatrician, the psychiatrist in modification of electric shock therapy complications by the use of muscle relaxants, and the internist in the respiratory management of polio patients have been as rewarding as those outlined in this discussion of the surgical patient with heart disease, but are not within the scope of this presentation.

Summary

The anesthetic management of patients with heart disease should include: (a) adequate preoperative preparation by the medical team and the patient; (b) minimum preoperative medication; (c) awareness of hazards of induction of and recovery from anesthesia; (d) effects of position changes;

(e) the least amount of pharmacological agents conducive to the surgical procedure; and (f) continuous expert attention to detail, before, during, and after the operation.

References

Adriani, John. Selection of Anesthesia; the physiological and pharmacological basis. C. C Thomas, Springfield, Ill., 1955.

Adriani, John. Some Causes of Cardiac Arrest. Journal of the Louisiana State Medical Society 107:219, June 1955.

Altschule, M. D. Physiology in Diseases of the Heart and Lungs. Harvard Univ. Press, 1954.

Brown, A. I. P., Sellick, B. A. Anesthesia for cardiac surgery, Brit. Med. Bull. 11:174-177, Sept., 1955.

Brown, S. Anesthesia for patients with cardiac disease. South. Med. J. 48:802-810, Aug., 1955.

Campbell, D. C., Jr., Langston, H. G. Intrathoracic surgical procedures in patients past the age of 60. J. Am. Geriat. Soc. 3:330-336, 1955.

Casten, D. F., Bardenstein, M. Cardiac arrest in children. Bull. Hosp. Joint Dis. 16:13-21, 1955.

Dillon, J. B. and Darsie, M. L. Oxygen for acute respiratory depression due to administration of thiopental sodium. J.A.M.A. 159:1114, Nov. 12, 1955.

Dodd, R. B. Anesthesia for the elderly. Am. Surg. 21:262-267, Mar. 1955.

Dripps, R. D. The anesthetic management of mass casualties. Lectures, Walter Reed Army Institute of Research, Washington, D.C., 1955-56.

Dugan, D. J., Sadusk, J. F., Jr., and Samson, P. C. The Responsibility of the General Thoracic Surgeon in Cardiac Surgery. Dis. of the Chest, 29:153-165, Feb. 1956.

Herrmann, G. R. Diseases of the heart and arteries, Anatomical and functional disturbances of circulation. The C. V. Mosby Co., St. Louis, 4th Ed., 1952.

Hershey, S. G., et al. An evaluation of the protective action of autonomic blocking agents in peripheral circulatory stress. Anesthesiology 15:589, 1954.

Heymans, Corneille, Introduction to the Regulation of Blood Pressure and Heart Rate. C. C Thomas, Publisher, Springfield, Ill., 1950.

Hickcox, C. B. and Tovell, R. M., Hartford Hosp., Conn. The Anesthesiologist in the Medical-Surgical team, W.Va. Med. J. 52:41, Feb. 1956.

Johnson, J., and Kirby, C. K., Univ. of Penn., A Handbook of Operative Surgery: Surgery of the Chest. Year Book Publishers, Inc., 1952.

Kepes, E. R., Livingston, M., Escher, D. J. Management of children during cardiac catheterization with inhalation anesthesia. Curr. Res. Anes. 34:299-306, 1955.

Mendelsohn, D., Jr., and Monheit, R., Philadelphia, Electrocardiographic and Blood-Pressure Changes During and after Biliary Tract Surgery. N.E. J. Med., 254:307-313, Feb. 16, 1956.

O'Donnell, J. A., McDermott, T. F. Anesthesia problems of surgical corrections of aortic insufficiency. Anesthesiology, 16:343-354, May, 1955.

Salman, O. L., Jr., Schwartz, S. P. Effects of vasoconstrictors used in local anesthetics in patients with diseases of the heart. J. Oral Surg. 13:209-313, July, 1955.

Schein, C. J., and Hurwitt, E. S. Recent Advances in Surgery of the Heart and Aorta, 1955. N. Y. State J. Med. 56:524, Feb. 15, 1956.

Shidler, F. B. Fluid and Electrolyte Management in Surgical Patients. Surg. Clin. N. Amer., 1954, p. 1231.

Weiss, E., Emotional Factors in Cardiovascular Disease. Springfield, Ill., 1951.

Glycogen Disease*

By

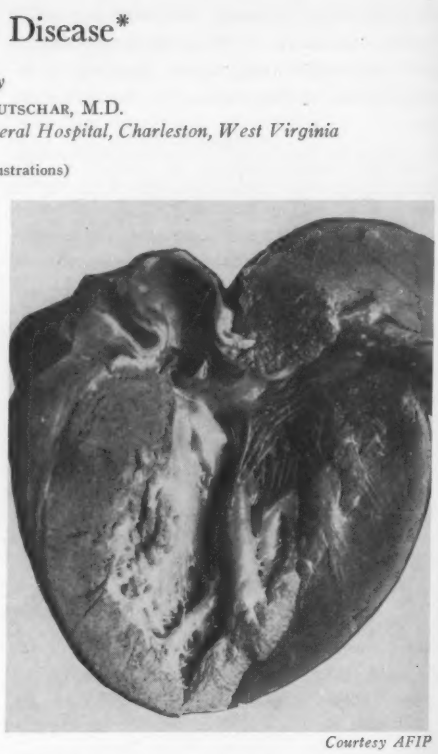
WALTER G. J. PUTSCHAR, M.D.

Department of Pathology, Charleston General Hospital, Charleston, West Virginia

(With 5 illustrations)

I WISH to discuss this rather rare entity because it offers a great number of clinical and biochemical problems in addition to the ordinary pathological ones. Since the glycogen storage disease group as a whole is a relatively recent contribution and comes entirely from pathological laboratories, we shall begin with the pathological aspects before discussing the clinical findings.

Von Gierke in 1929 first described two cases of what is now known as the classical or hepatic type of glycogen storage disease, in which in children an extreme enlargement of the liver and also to some degree of the kidneys is seen, due to abnormal storage of glycogen. In 1932 I had the opportunity of autopsying a four month old child in whom the clinical diagnosis of idiopathic cardiac hypertrophy had been made. The child died in cardiac failure complicated by bronchopneumonia. The autopsy revealed the cardiac enlargement to be due to excessive glycogen deposition in the myocardium. It is questionable now whether this cardiac type of glycogenosis is really related to the hepatic type, or whether it represents an entirely separate disease entity. It is a much rarer condition than the hepatic glycogenosis of von Gierke. To this date approximately 200 cases of the hepatic form of classical von Gierke's disease have been described, while only about 20 cases of authenticated cardiac glycogen storage disease have come to observation. In 1932, the year I published this case, Pompe in Holland independently reported a similar one. We came to the same conclusions without knowing of each other's observations.



Courtesy AFIP

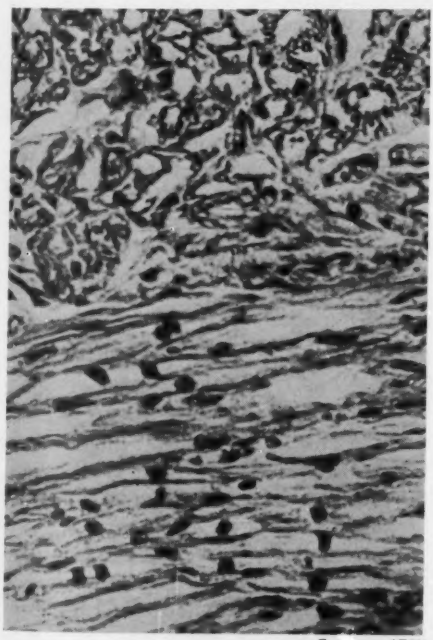
FIG. 1. Cardiac type of glycogenosis, view into the uniformly thickened left ventricle (4 mos. white female).

The morphological findings are grossly and microscopically very characteristic. The heart of this four month old child weighed 110 grams, about 3 to 5 times normal weight for this age. A view into the opened left ventricle demonstrates the globular appearance of the heart with a very rounded apex and with tremendous diffuse and uniform thickening of the myocardium, due to storage of glycogen (Fig. 1). Apparently a maximum of about ten per cent of dried weight of myocardium can be represented by glycogen; anything beyond that is incompatible with life. The myocardium of the right ventricle is also uniformly very much thicker. Measurement showed a maximum thickness of 21 mm. on the left and 12 mm. on the right. The thickening is not as conspicuous

* Presented at the Post-Graduate Seminar on Diseases of the Heart. Held at the Armed Forces Institute of Pathology, Washington, D.C., May 14-17, 1956, and Co-sponsored by The American Heart Association, Inc.

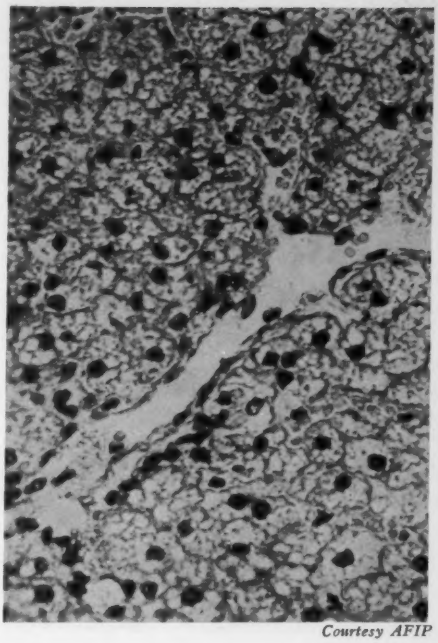
in the atrial as in the ventricular areas.

The microscopic picture is quite characteristic and extremely striking so that on first glance one is not aware of seeing a section of myocardium; but to those who are familiar with some aspects of microscopic botany the similarity to a section of plant material is marked. The main feature is the uniformity of the distribution of deposited glycogen throughout the entire myocardium. There is no evidence of necrosis or interference with pliability of the myocardium. The myocardial nuclei all stain well. The myocardial fibers show a rather large central space, occupied by the glycogen, not visible in the ordinary hematoxylin-eosin stain, which pushes the myofibrils to the periphery of the muscle fiber (Fig. 2). This is even better appreciated on the cross-sections where the myofibrils surround the central areas occupied by the glycogen-carrying vacuolated material. The marked similarity to the Purkinje type fibers of the conductive bundle is apparent. Both resemble some of the early embryonic appearances of myocardium.



Courtesy AFIP

FIG. 2. Myocardium in cardiac type of glycogenosis. Note hollow myocardial fibers due to central deposition of excessive glycogen (4 mos. white female).

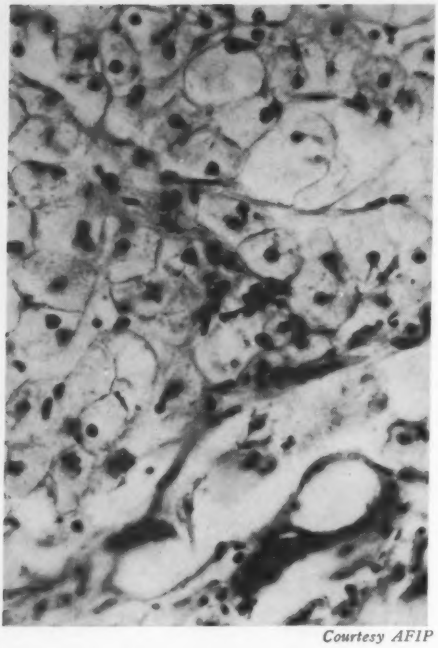


Courtesy AFIP

FIG. 3. Liver in cardiac type of glycogenosis. Note moderate glycogen storage in liver cell cytoplasm (4 mos. white female).

In this original case, of course, the existence of cardiac glycogenosis was unknown at the time of autopsy. We were not aware that we were dealing with a glycogen problem and did not fix in alcohol, but three weeks later we found a considerable amount of glycogen extracted in the formalin fixative, and some still in the myocardium which took the Best carmine stain.

The liver in this case, and in all cases of the cardiac type, is only moderately enlarged. It does show a moderate increase in cytoplasmic glycogen, emphasizing the plant cell-like pattern of the liver cells (Fig. 3). No intranuclear liver glycogen is present in glycogenosis. Even after three weeks some stainable glycogen was found in the liver cells;



Courtesy AFIP

FIG. 4. Liver in hepatic type of glycogenosis. Note extreme glycogen storage in liver cell cytoplasm (3 yr. white male).

more still was present in the reticulo-endothelial component, the so-called Kupffer cells of the liver. This has been seen since in other cases.

By contrast in a liver biopsy of a three year old boy with hepatic or classical von Gierke's disease, the liver is the main locus of the glycogen deposition. One finds here extreme enlargement of the liver cells with a massive amount of cytoplasmic glycogen (Fig. 4). The liver also already shows beginning cirrhotic changes as seen in some of these children. This time we were aware of the situation and fixed part of the tissue in alcohol so that fully representative Best carmine stains could be obtained, to demonstrate that the liver lobules are loaded to maximum capacity with glycogen.

The kidney of the cardiac type shows no appreciable enlargement. Deposition of glycogen is fairly limited at the microscopic level. In the Best carmine stain some glycogen could be found in capsular epithelium and in glomerular epithelium as well as in some of the tubules. By contrast, in a section Dr. von Gierke gave me of his original hepato-nephromegalic case, in which the kidneys were about five times normal weight, extremely massive deposition of glycogen was apparent in all the tubules and in the glomerular epithelium by Best carmine stain.

Di Sant' Agnese, Anderson and Mason showed that in the cardiac type the distribution of glycogen is rather diffuse in many of the organs and not necessarily grossly apparent. They found in the skeletal muscle fibers a pattern of glycogen distribution very similar to that which we saw in the myocardium.

Let us summarize the autopsy findings. In the hepatic form the deposition of glycogen is centered essentially around the grossly enlarged liver and kidneys. In the cardiac form the distribution of glycogen in addition to excessive myocardial deposition is very diffuse. The skeletal musculature, and sometimes the tongue, are the seat of marked glycogen deposition. In six of the twenty cases described lingual deposits were so extensive that the tongue was macroglossic and protruding, suggesting the clinical diagnosis of either mongolism or cretinism without either being present. Glycogen was also found in the smooth muscle and in many other organs, including the nervous system.

Clinically the two types, or possibly we should rather say the two diseases, are quite different. The cardiac type and the hepatic type have, however, one thing in common: frequency of familial incidence indicating the importance of heredity. There is at present, however, no observation of the occurrence of both diseases in the same family.

In the cardiac type the onset is almost immediate after birth. The prognosis is extremely poor. There is no completely bona fide case of survival beyond the first year of life. Most die in the first half year of life of cardiac failure complicated by pulmonary infections. X-ray shows a globular heart without any distinctive characteristics. The pic-

ture is not in itself diagnostic; but the absolute roundness in connection with the clinical findings is a very striking feature. These findings consist of markedly impaired nutrition, fretfulness, tachypnea, and attacks of dyspnea and cyanosis, particularly on feeding, and arouse the suspicion of this condition. The clinically and radiologically suspected diagnosis of cardiac glycogenosis can be made at this time by muscle biopsy. The physician should request a combined study for glycogen chemically and histologically, which will usually yield a diagnosis.

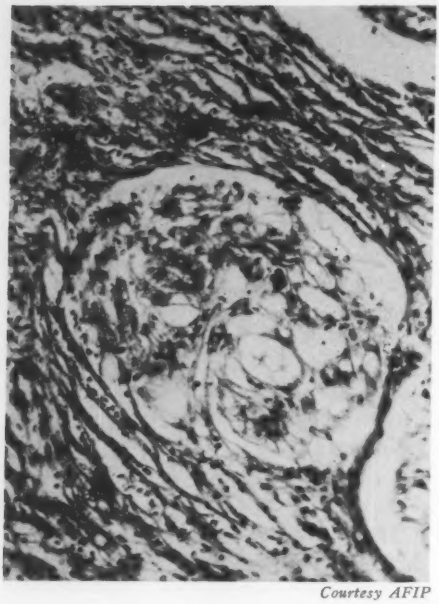
Electrocardiographic features are not diagnostic. Five cases from the total of twenty have had abnormal electrocardiograms, which showed essentially a low takeoff and inversion of the T-wave with either left or no axis deviation. This is, of course, abnormal in the first half year of life because at this age a physiological right axis deviation should be present. The picture is not diagnostic; it could as well be an aberrant left coronary artery arising from the pulmonary, tricuspid atresia, or endocardial fibrosis.

Comparison of the clinical findings in the hepatic and cardiac forms is probably of some importance because the two diseases have been too much confused in the past. I shall follow the outline of di Sant' Agnese and co-workers. The onset of the hepatic type is early in life but not immediate; that of the cardiac type is almost immediate, certainly within the first two months. Physical findings in the hepatic type include hepatic enlargement and physical retardation; in the cardiac type marked cardiomegaly, cyanosis, and dyspnea are seen. Nutrition in the hepatic type is frequently fairly adequate, and even obesity may be found, while in the cardiac type malnutrition is always a leading symptom. Hypoglycemia is usually present in the hepatic type; if the children are old enough to express themselves, they frequently show a pronounced hunger for carbohydrate of any kind. In contrast hypoglycemia is always absent in the cardiac form. The patient with the hepatic form of the disease has a life expectancy of at least several years, and there are some observations suggesting that the condition grows milder with age. In the cardiac type death usually occurs between the ages of one and eight months, although a case of eleven months' survival has been described. Death in the hepatic type is usually caused by intercurrent infection or acidosis because these children live essentially by burning fat rather than carbohydrate. The cause of death in the cardiac type is cardiac failure or its complications.

The metabolic aspects of both diseases deserve some elaboration. Very characteristic differences in carbohydrate metabolism are seen in the two types of disease. We have discussed the extent and location of the glycogen deposits in the different organs. Hypoglycemia is present in the hepatic type and absent in the cardiac form. Resting blood lactate is usually elevated in the hepatic type and normal in the cardiac. Glycemic response to epinephrine cannot be elicited in the hepatic type, but is normal in the cardiac variety. The same is true of lactic acid. Glucose tolerance curve may show a high rise in the hepatic type but be perfectly normal in the cardiac. The blood glycogen is always increased in the hepatic but is normal in the cardiac form. Finally post-mortem autolysis of glycogen is virtually absent in the hepatic form, but apparently normal in the cardiac.

The serum lipids as expected are usually increased in the hepatic type because the energy metabolism is based essentially on the utilization of lipids and fat; in the cardiac type the energy metabolism is normal. The serum cholesterol is usually elevated in the hepatic type, but normal or low in the cardiac. Ketonuria on fasting is usually very pronounced and ketosis actually is frequently the cause of death in the hepatic type, while in the cardiac type ketosis is not observed.

The underlying metabolic abnormality and the pathophysiologic mechanism are only partly known. In the hepatic form of the disease various mechanisms can be at fault. In the classical form described by von Gierke the glycogen is structurally normal, but there is an enzymatic defect consisting of a defi-



Courtesy AFIP

FIG. 5. Multiple "spider cell rhabdomyomas" of myocardium in tuberous sclerosis (23 hrs. white, sex not stated).

ciency of glucose-6-phosphatase. In other types of the hepatic form structurally abnormal glycogen with partly unusually long, partly unusually short side chains has been demonstrated, indicating deficiency in branching or debranching enzyme respectively. In cardiac glycogenosis the chemistry of the glycogen stored is not abnormal and no enzyme deficiency has been demonstrated. The actual mechanism of this metabolic abnormality is at present unknown. The possibility has been suggested that in this condition carbohydrate cannot be converted into fat. This would explain the extremely poor nutritional state of these infants, while unusable glycogen accumulates in the myocardium. A similar situation seems to exist in the occasional observation of glycogen storage in the skeletal muscle without involvement of the myocardium.

I wish to call attention finally to the fact that there has been some confusion in the literature regarding the tendency to call any condition glycogen storage disease which shows an increase of glycogen in the tissues, particularly in the myocardium. There are abnormal increases of glycogen in the myocardium in a number of conditions other than glycogenosis. For instance, I have seen a considerable increase of glycogen in the myocardium of a one month old child with transposition of the arteries, which I believe was due to the aorta's failure to carry an adequate amount of oxygenated blood. We know also that myocardial glycogen accumulation occurs in coronary artery disease.

One condition that should be mentioned briefly has confusingly been called localized glycogenosis of the myocardium. This is a condition in which a congenital tissue malformation of the myocardium produces multiple nodules of rather glycogen-rich muscle fibers (Fig. 5). This lesion was originally described by Recklinghausen as disseminated rhabdomyoma and is, as we now know, part of the rather complicated tissue malformations (hamartomas) found in tuberous sclerosis or Bourneville's disease. Some instances of diffuse glycogen deposition in the myocardium, wrongly called rhabdomyoma, were seen before my case. "Diffuse rhabdomyoma" of the heart is certainly glycogenosis, but the disseminated rhabdomyomas or spider-cell tumors have nothing to do with it.

In closing I would like to leave you with the thought that until we know more it might be better to speak about glycogen storage *diseases* rather than glycogen storage *disease*, and keep the cardiac and hepatic forms separate. Particularly we should not assume that all cases of idiopathic hypertrophy of the myocardium and all cases of increased myocardial glycogen belong to this disease.

REFERENCES

[1] Von Gierke, E.: Hepato-Nephromegalia Glygogenica (Glykogen-speicherkrankheit der Leber und Nieren). Beitr. z. path. Anat. u. z. allg. Path., 82:497, 1929.

[2] Putschar, W.: Ueber Herzvergroesserung bei Glykogenose des Myokards. Med. Ges. Goettingen, Jan. 21, 1932, Muench. Med. Wochschr., 1499, 1932.

[3] Putschar, W.: Ueber angeborene Glykogen-

speicherkrankheit des Herzens—"Thesaurismosis glykogenica" (von Gierke). Beitr. z. path. Anat. u. z. allg. Path., 90:222, 1932.

[4] Pompe, J. C.: Over idiopatische hypertrophie van het hart. Nederl. tidschr. v. geneesk., 76:304, 1932.

[5] Pompe, J. C.: Hypertrophie idiopathique du coeur. Ann. d'anat. path., 10:23, 1933.

[6] Di Sant' Agnese, P. A., Andersen, D. H., Mason, H. H., and Bauman, W. A.: Glycogen storage disease of the heart, I. Ped., 6:402, 1950.

[7] Di Sant' Agnese, P. A., Andersen, D. H., and Mason, H. H.: Glycogen storage disease of the heart, II. Ped., 6:607, 1950.

[8] Cori, G. T.: Glycogen structure and enzyme deficiencies in glycogen storage disease. Harvey Lect., 145, 1952-53. New York, Acad. Press, 1954.

[9] Schulman, J. L., and Saturen, P.: Glycogen storage disease of the liver, I. Ped., 14:632, 1954.

[10] Cori, G. T., and Schulman, J. L.: Glycogen storage disease of the liver, II. Ped., 14:646, 1954.

[11] Andersen, D. H.: Familial cirrhosis of the liver with storage of abnormal glycogen. Lab. Inv., 5:11, 1956.

Clinical Aspects of Rheumatic Heart Disease*

(With Special Reference to Mitral Stenosis)

By

W. Proctor Harvey, M.D.

Director of the Heart Station, Georgetown University, Washington, D.C.

(With eight illustrations)

THE clinical aspects of rheumatic heart disease represent a subject so broad that it obviously cannot be covered in the time allotted this morning. Therefore, only a few of the more pertinent points will be discussed.

Because of the recent advances in the treatment of rheumatic heart disease, particularly surgical treatment, it has become much more than academic interest to accurately diagnose the specific valvular lesion. For example, when the surgeon operates for mitral stenosis he is naturally dependent upon the correct preoperative diagnosis; unfortunately this has not always been the case as other conditions may mimic or be confused with mitral stenosis. It is worthy of re-emphasis to stress again basic fundamental points in recognizing some of the rheumatic valvular lesions.

Many new specialized techniques have made great advances in our knowledge and improved our accuracy of diagnosis. These include left and right heart catheterization, angiocardiography, ballistocardiography, phonocardiography, electrocardiography, etc. However, all too often there has been the tendency to forget the necessity of a careful history and physical examination. As a rule, in the average patient having a cardiovascular evaluation we learn most from the history. Second in importance is the physical examination.

From the history we often get our first clue of mitral stenosis. In every patient a detailed history concerning the possibility of rheumatic fever should always be searched for, because if positive, there is an approximate 50% chance of finding a rheumatic valvular lesion in that particular patient. Even if there is not a definite history of specific rheumatic fever, questions concerning "growing pains," joint pains, nose bleeds, chorea, may be the first lead to put one on the alert to listen even more carefully for the rumble of mitral stenosis. On the other hand, approximately half of the patients having definite mitral stenosis have had no previous history of rheumatic fever. The tight mitral stenosis causing symptoms should not be overlooked, for the surgeon can do most for this particular valvular deformity. Results are excellent and the risk is minimal. However, even today a significant number are still being overlooked. In fact, only yesterday two such examples were called to my attention. One, a patient in a sanatorium diagnosed tuberculosis because of hemoptysis; another had X-ray therapy for pulmonary malignancy, which in actuality was enlarged pulmonary arteries. Both of these patients had mitral stenosis.

A history of dyspnea needs careful evaluation. It is worthy of emphasis that there is often a difference in history obtained in a patient with mitral stenosis as opposed to the one with aortic valve involvement. We have been impressed that women with mitral stenosis are less able, because of dyspnea, to perform their usual household duties, such as sweeping, cleaning, making beds, ironing or any effort involving use of their arms. These are usual household duties which ordinarily would not cause any difficulty. In addition, walking up only one flight of stairs is likely to result in prompt unusual exer-

* Complete lecture "Clinical Aspects of Rheumatic Heart Disease" was presented at the Post Graduate Seminar on Diseases of the Heart. Held at the Armed Forces Institute of Pathology, Washington, D.C., May 14-17, 1956, and Co-sponsored by The American Heart Association, Inc.

tional dyspnea causing the patient to stop and rest. This history, plus that of rheumatic fever immediately points to that of mitral stenosis. The patient with aortic valvular disease is more likely to perform such duties or activities and if symptoms do occur, are more likely to come afterwards.

Hemoptysis might be a presenting feature of mitral stenosis, as in the patient cited above, which might be misinterpreted as tuberculosis. Unexplained hemoptysis should always suggest mitral stenosis until ruled out.

To illustrate the importance of history, I was amused by a patient we saw at Bethesda Naval Hospital approximately one and one-half years ago. This lady was watching Medic, a T-V show. Apparently a case of mitral stenosis was the feature of that particular show, portraying a woman complaining of exertional type of dyspnea particularly on climbing stairs. Our patient so paralleled the T-V version she turned to her husband and said in effect, "I've got those symptoms myself." Her husband tried to reassure her but she felt convinced she had the same symptoms as did the actress on the television. She then went to one physician who apparently found no evidence of heart disease. However, another physician was consulted who confirmed her suspicion of mitral stenosis. She subsequently came to Bethesda Naval Hospital where she was noted to have classical symptoms and findings of a tight mitral stenosis, which was successfully operated upon.

Occasionally a malar flush might be the first clue on physical examination to suspect mitral stenosis. Of course some people have it in the absence of mitral stenosis, as illustrated by a pregnant woman seen recently whose obstetrician wanted mitral stenosis ruled out because of an unusually prominent malar flush. No heart disease was present and her "malar flush" was merely a healthy complexion.

Our first suspicion, therefore, of mitral stenosis may come from the history. This may usually be confirmed on the physical examination where auscultation of the heart is of prime importance. In discussing the auscultatory findings of mitral stenosis, it is particularly appropriate to stress the analogy of listening to music. For example, if Beethoven's Eighth Symphony would suddenly be heard in this auditorium I could ask "how many hear the music?" Naturally, everyone would answer in the affirmative. On the other hand, if I asked "how many heard specifically a violin, drum, or horn?," few would have done so. However, if we replayed the music and we set about to pick out a particular instrument we could readily do so. In the same way we must auscult the heart. We listen specifically to the various components of the heart cycle. At the apex the first heart sound is carefully noted as to whether it is loud, faint, or is changing in intensity. The second heart sound, particularly over the pulmonic and aortic areas, likewise must be carefully ausculted in a similar fashion. Then sounds in systole, sounds in diastole (opening snap, gallop, etc.), murmurs in systole and finally, murmurs in diastole. This actually takes only a few seconds with each component of the heart cycle, and is a fundamental principle in properly listening to a heart. Mitral stenosis is an excellent illustration of the importance of listening specifically. Our first clue to its presence may come from the sounds of mitral stenosis: namely, the loud first sound, the accentuated pulmonic component of the second, and the opening snap (Fig. 1). An accentuated first heart sound is almost always present in tight mitral stenosis and this single finding in the absence of a tachycardia suggests mainly two things: mitral stenosis or a short P-R interval.

An accentuation of the pulmonic component of the second heart sound likewise is frequently present. The combination of the loud first sound plus the prominent pulmonic second (Fig. 1) further focuses our attention on the possibility of mitral stenosis.

Then there is the third sound of mitral stenosis, the so-called opening snap (Figs. 1, 2, 5, 6). Probably the term *opening snap*

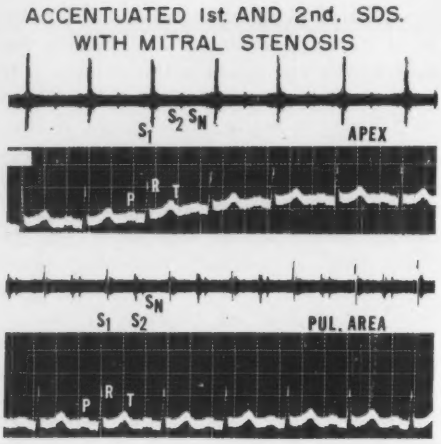
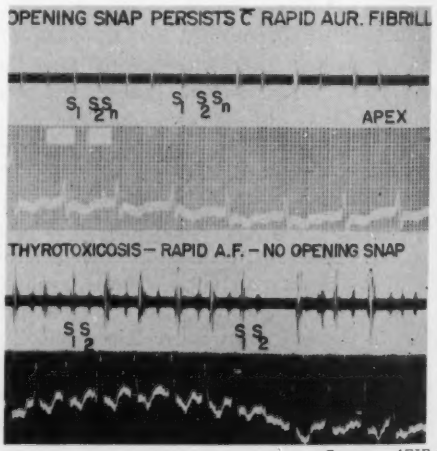


FIG. 1. Upper tracing: Apex. Note loud first sound (S_1)—Opening snap (S_n). Lower tracing: Pulmonic area. Accentuation of pulmonic component of second sound (S_2) present. Both first and second sounds in this area are prominent. (S_1 "retouched" to show loud S_1 which reproduced poorly from original phonocardiogram.)

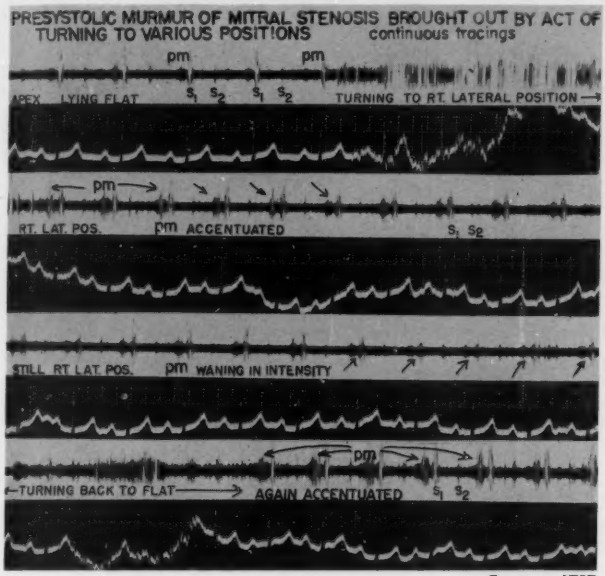
is not the ideal one because it is frequently confused as meaning the first sound. This is due to the commonly described *"snapping* first sound" with mitral stenosis. To avoid this confusion, perhaps a better term therefore, is the third sound of mitral stenosis. However, in all probability, the term "opening snap" is now firmly fixed in our nomenclature. Not uncommonly the third sound of mitral stenosis, or opening snap, is the first auscultatory clue that mitral stenosis is present. This sound in early diastole is heard in the great majority with mitral stenosis and is generally louder, and therefore more easily detected, in the presence of a "tight stenosis." It persists with auricular fibrillation even though the rate may be rapid with a tachycardia (Fig. 2). As will be discussed later, a diastolic rumble may be quite difficult or impossible to hear at the more rapid ventricular rates, but the finding of the opening snap suggests the correct diagnosis which will become more evident as the rate slows.

Although these auscultatory *sounds* characteristic of mitral stenosis (accentuated first and pulmonic component of the second, and opening snap) are heard, the diagnosis should be reserved until in addition the typical rumble of mitral stenosis is auscultated. Several points are worthy of emphasis to aid in detecting the diastolic rumble of mitral stenosis. First, one should locate by palpation a maximum apical impulse as the rumble is almost always best heard in this localized spot (which may be no larger in size than a quarter or a silver dollar). The bell of the stethoscope should then be placed very lightly over this area gently making an air seal with the bell piece of the stethoscope contacting the skin of the chest wall. The next step which is of great importance and frequently neglected, is to listen *as the patient turns* to the left lateral position. The importance of the act of turning in "bringing out" the rumble of mitral stenosis has not been adequately stressed. In fact, it is of even more importance than the positioning of the patient which has been so well emphasized in the past. Figure 3 illustrates the necessity of listening *as the patient turns,* where the diastolic rumble was accentuated immediately during the first beats coincident with turning from the flat to the right lateral position and also from the right lateral position to flat again. The same accentuation of



Courtesy AFIP

FIG. 2. Two cases with auricular fibrillation. Upper tracing: Mitral stenosis. First clue as to diagnosis was opening snap (S_n) as rumble was not noted in this particular area.



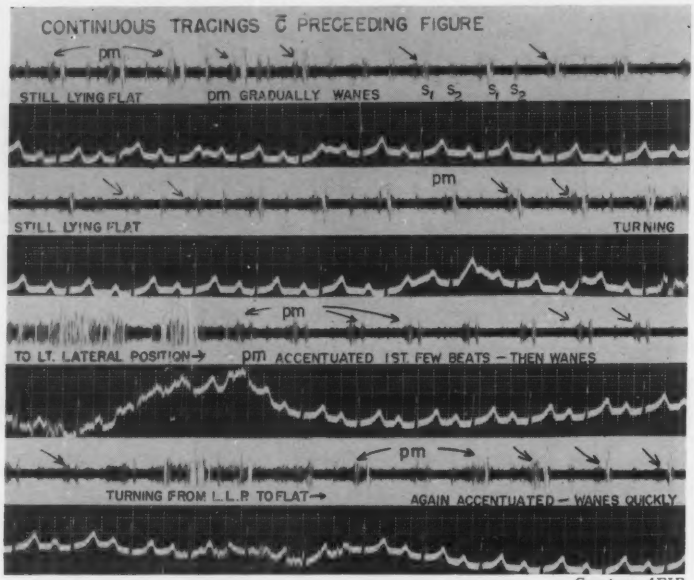
Courtesy AFIP

FIG. 3a. (Continuous tracings at apex) "Tight" mitral stenosis. Note presystolic murmur (PM) immediately becomes loudest (2nd strip) on turning from the flat to the right lateral position. Murmur then quickly decreases in intensity (3rd strip) but is accentuated again on turning back to the flat position (4th strip).

the rumble occurred on turning from the flat to the left lateral position and also increased in intensity on turning from the left lateral position to flat again. Sometimes this diagnostic rumble signifying mitral stenosis is best heard during the first five to ten beats coincident with turning and then wanes in intensity thereafter. This explains a situation a number of us have experienced at some state of our medical training. For example, on ward rounds where a group of students or physicians are discussing a particular patient, the instructor examines the patient, turns him to the left lateral position, comes away saying, "there is a typical loud rumble of mitral stenosis." As our turn comes up to listen to the patient (still in the left lateral position), no rumble is evident. The instructor then "wonders" about us and we in turn "wonder" about him. We think he *didn't* hear it, and he thinks we *couldn't* hear it. Actually, as illustrated in Figure 3, this discrepancy is easily explained. The instructor, or first observer, listened as the patient turned, or immediately thereafter, when the rumble was evident. The murmur had decreased significantly by the time the next observers listened. In order of importance, therefore, in utilizing this maneuver to elicit the rumble of mitral stenosis, of first importance is *the act of turning;* and second, the *position*, the best being the left lateral position.

Other maneuvers can be used to accomplish the same effect. For example, simply having the patient cough five or six times and listening immediately thereafter may produce a similar accentuation of the diastolic rumble as shown in Figure 4. Having the patient rapidly exhale and inhale deeply for a few times can also be effective. The use of amyl nitrite inhalation is particularly useful to produce a more prolonged accentuated diastolic rumble thereby enabling a larger group to hear this auscultatory finding. If necessary, a slight amount of exercise may likewise demonstrate a similar effect.

The ventricular rate is a major factor in determining whether the murmur of mitral stenosis will be well heard or not (Figs. 5 and 6), for the murmur is often poorly heard at the two extremes. At a slow rate, for example, 40 to 50, a short, faint rumble may or may not be heard, and if present



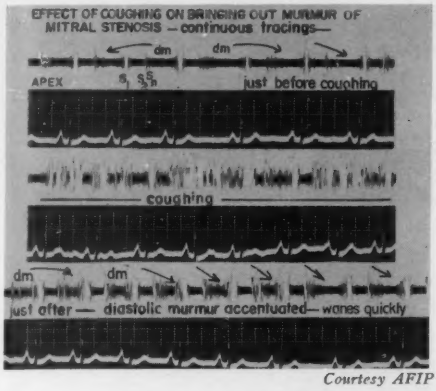
Courtesy AFIP

FIG. 3b. (Continuous with Fig. 3a). Murmur (PM) then becomes fainter (first and second strips) but is again accentuated on turning to the left lateral position (3rd strip), quickly wanes but once more is accentuated on turning from the left lateral position back to flat (4th strip) where only the first few beats thereafter produce the loudest diastolic murmur.

usually is in the earlier part of diastole following the opening snap. At normal rates of 70 to 80, the diastolic rumble may be readily detected but is even better, or often optimally, heard with a heart rate of 90 to 110. A further increase in rate then generally becomes more difficult to auscult the diastolic murmur. At the upper ranges above 150 one may be unable to hear it or if heard, may be greatly diminished in intensity.

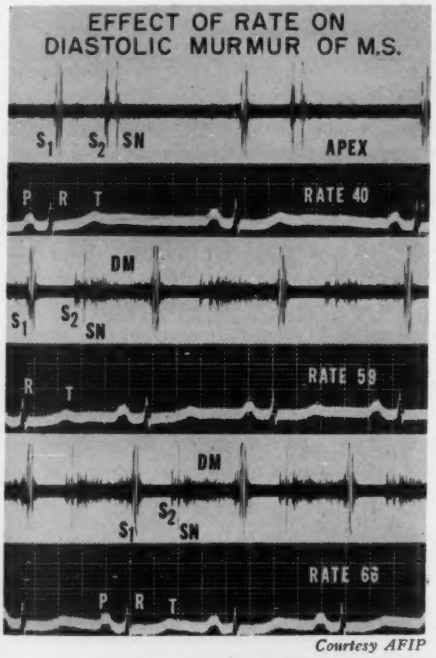
Occasionally documented cases of tight mitral stenosis are reported where no murmur has been heard, regardless of rate. The absence of the murmur in such cases would obviously be related to blood flow across the stenotic mitral valve and a factor such as advanced cardiac decompensation could so reduce flow as to alter the murmur. In our own hospital we have likewise observed proven cases of advanced mitral stenosis where at times no diastolic rumble was evident. On other occasions, however, in the same patient, a definite typical diastolic rumble was heard. It is possible, therefore, that a single examination may not reveal the typical murmur, but if one has the opportunity to follow such a patient he is likely at some time to detect it. Such cases as these that might derive benefit from surgery should therefore always be kept in mind. In the absence of the diagnostic rumble of mitral stenosis, the auscultatory sounds should serve sufficient notice that repeat follow-up examinations are necessary to rule out this correctable valvular lesion. X-ray and fluoroscopy of the heart can be especially helpful in this instance. If calcium is seen in the mitral valve, this would practically establish the diagnosis of mitral stenosis. The technique outlined by Sosman should be followed, (1) remembering to accommodate with dark glasses for 20 to 30 minutes prior to fluoroscopy. In our experience a calcified mitral valve is seen in approximately one-fourth to one-third of the cases with mitral stenosis being evaluated for commissurotomy.

A final group of patients should be mentioned who have symptomatic mitral stenosis



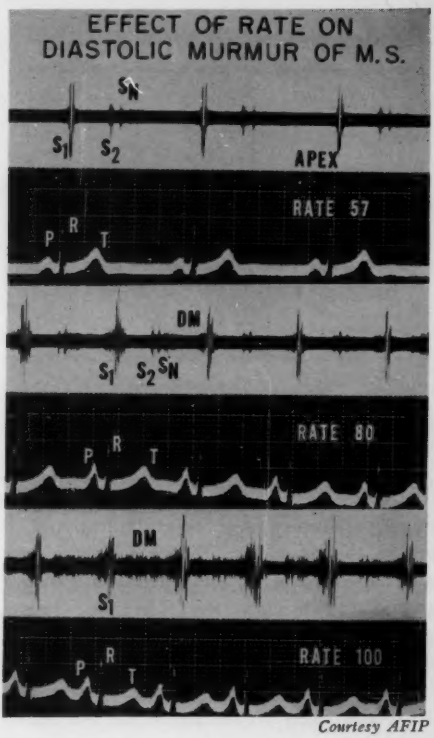
Courtesy AFIP

FIG. 4. (Continuous tracing) Upper Tracing. Apex. Note loud first sound (S_1) second (S_2) and opening snap (S_n) followed by diastolic rumble (DM). Coughing (5 or 6 times) in 2nd strip immediately followed by great accentuation of diastolic murmur (DM) (third strip) which begins to wane after the 6th beat.



Courtesy AFIP

FIG. 5. Upper tracing: Ventricular rate 40. Note loud first sound (S_1) second sound (S_2) and prominent opening snap (S_n). Middle tracing: Rate 59. Diastolic rumble (DM) now easily heard. Lower tracing: Rate 66. Rumble (DM) still better heard.

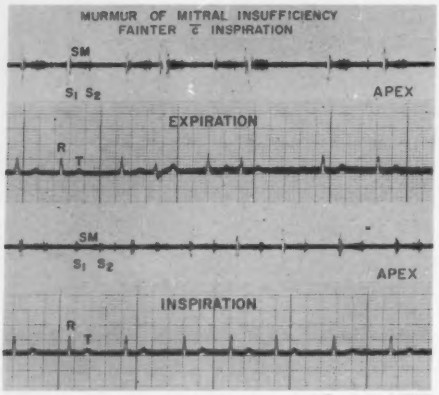


Courtesy AFIP

FIG. 6. Upper tracing: Ventricular rate 57. Note loud first sound (S_1), second sound (S_2) and opening snap (S_n) followed by faint diastolic rumble (DM). Middle tracing: Ventricular rate 80. Diastolic murmur (DM) better heard. Lower tracing: Rate 100. Murmur (DM) (filling all of diastole) now best heard.

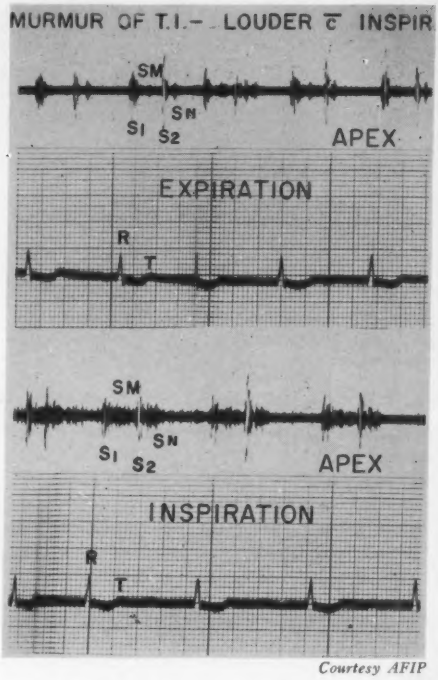
but are denied surgery because of tricuspid insufficiency masquerading as mitral insufficiency. We have had the opportunity to evaluate such patients previously denied surgery for mitral stenosis because of a suspected significant mitral insufficiency. However, after re-evaluation of these patients it was apparent that the systolic murmur of tricuspid insufficiency was present and was being confused with mitral insufficiency; operation was subsequently performed revealing a tight stenosis of the mitral valve with no significant insufficiency. It is obvious that we must be on the alert for this murmur of tricuspid insufficiency.

In patients with mitral stenosis but having significant or severe associated mitral insuf-



Courtesy AFIP

FIG. 7. Rheumatic Mitral Insufficiency. Note decrease in systolic murmur (SM) from expiration (upper tracing) to inspiration (lower tracing).



Courtesy AFIP

FIG. 8. Mitral Stenosis and Tricuspid Insufficiency. Systolic murmur (SM) of tricuspid insufficiency increases on inspiration (lower tracing). Patient had surgical corrected proven tight mitral stenosis with no mitral insufficiency.

ficiency, surgery is a contraindication. To aid in the diagnosis of mitral insufficiency and not confusing it with the murmur of tricuspid insufficiency the following clinical points have been useful. The murmur of severe mitral insufficiency has generally been loud (over Grade III—grading on basis I to VI), and likely to radiate to the left axilla and left lung base. It decreased in intensity on inspiration (Figure 7) (rather than increasing as with tricuspid insufficiency) (Figure 8).

The giant left atrium and left ventricular enlargement as noted on physical examination, electrocardiogram or X-ray and fluoroscopy would likewise be points suggesting mitral insufficiency.

Therefore, a Grade III or IV systolic murmur in a patient with mitral stenosis should not be diagnosed as mitral insufficiency on this single finding alone. The possibility that this murmur could be that of tricuspid insufficiency should be entertained, and if so, this murmur characteristically increases on inspiration rather than decreasing. If other physical findings of mitral stenosis are present coupled with a history of unusual exertion coincident with effort the possibility of correctable mitral stenosis without significant insufficiency must be entertained. Further information can be obtained from electrocardiographic and X-ray studies. If necessary, left and right heart catheterizations may be performed which can aid in the diagnosis.

Needless to say, the total cardiovascular evaluation of any patient is of the utmost importance. This includes a careful and detailed history and also the electrocardiogram, fluoroscopy and X-ray, plus special laboratory tests when indicated. Dependence on one single aspect of the total evaluation will naturally lead to diagnostic errors.

Of all possibilities of valvular involvement by rheumatic fever, stenosis of the mitral valve has been the one most benefited by surgery. Because of this, the edited and published material taken from the lecture, "Clinical Aspects of Rheumatic Heart Disease" deals mainly with mitral stenosis. Space does not permit the inclusion of the discussion of the clinical aspects of the aortic and tricuspid lesions.

Pathology of Rheumatic Heart Disease*

By

IRA GORE, M.D.

Veterans Administration Hospital, West Roxbury, Mass.

(With 6 illustrations)

RHEUMATIC heart disease ranks with hypertension and coronary arteriosclerosis as one of the most frequent and serious forms of cardiac disorder. It is the leading cause of death during the 5 to 20 year period and ranks second to tuberculosis in the succeeding five years. The peak incidence accounting for two-thirds of all cases occurs in the school age decade 5 to 15 years; the rate varies from 3 to 14 cases per thousand affecting the sexes equally. Geographically, the frequency of rheumatic fever parallels that of streptococcal respiratory disease.[1,2]

Clinically the relation of acute articular symptoms and heart disease has been established for more than 150 years;[3] during the last half of this period the therapeutic benefits of salicylates have been appreciated.[4] While pericardial and endocardial involvement were recognized from the start it was not until 1879 that Goodhart[5] indicated the presence of myocardial inflammation whose specific character was described by Aschoff in 1904.[6]

Although von Glahn and Pappenheimer, 1926,[7] and Talalajew, 1929,[8] suggested it earlier, Klinge, 1931,[9] is generally credited with recognition of collagen degeneration as the initial morphologic change in acute rheumatic fever. This alteration occurring within the first few weeks consists of focal areas of swelling, homogenization, increased eosinophilia and refractility of connective tissue bundles which assume many of the staining characters of fibrin and is accordingly designated as fibrinoid. Silver stains show persistence of the reticulum, initially at least, so that the change must involve the supporting ground substance. Altschuler and Angevine[10] conclude that fibrinoid results from the precipitation of acid mucopolysaccharides, of which hyaluronic acid is a member, by basic proteins released in the vicinity of tissue damage. However, despite considerable investigation, the nature of the change is still unsettled. At this phase, cellularity is not increased and indeed the stromal cells observed are shrunken and pyknotic. Subsequently numbers of small mononuclear cells accumulate together with a few granulocytes. Further metamorphosis results in the formation of the diagnostically specific submiliary Aschoff nodule. (Fig. 1, 2, 3) The conspicuous but not sole cellular component is a large palely basophilic stromal cell with large hyperchromatic, frequently lobate, oc-

FIG. 1. Acute rheumatic myocarditis characterized by an Aschoff nodule involving the perivascular supporting stroma. Observe the swollen, smudgy and tinctorially altered collagen bundles which constitute fibrinoid necrosis; the conspicuous accumulation of large sometimes multinucleate histiocytic cells; and more peripherally, the less conspicuous nonspecific lymphocytic infiltrate.

*Presented at the Post-Graduate Seminar on Diseases of the Heart. Held at the Armed Forces Institute of Pathology, Washington, D.C., May 14-17, 1956, and Co-sponsored by The American Heart Association, Inc.

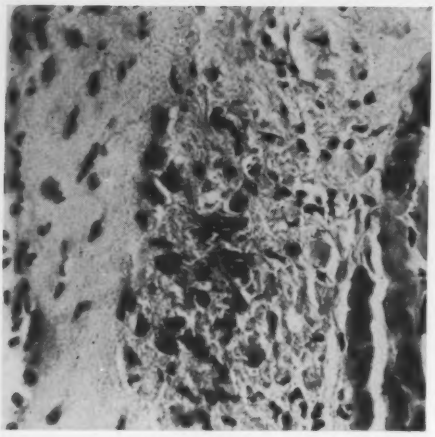


FIG. 2. Aschoff nodule within the left atrial endocardium. As in the preceding figure, the large mononuclear cells composing it are aggregated about a focus of fibrinoid necrosis. The tissue was obtained surgically from a patient with mitral stenosis; clinically there had been no evidence of active rheumatic carditis.

casionally multi-nucleate nucleus. Aggregations of these form an ovoid or spindle shaped nodule with a lamellated structure continuous with the fibers of the perivascular stroma in which they characteristically occur. Fibrinoid necroses are not invariably present,

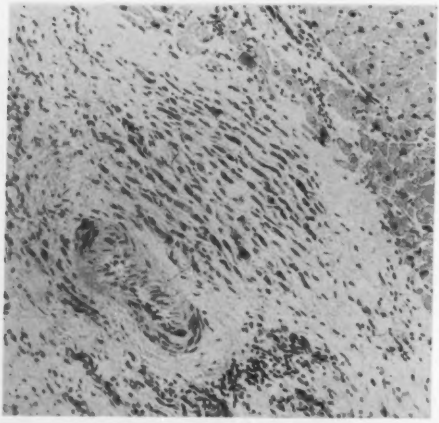


FIG. 3. Aschoff nodule exhibiting a lamellated structure; fibrinoid necrosis is not present. Some observers consider this to be an older type of lesion than the preceding figures. Note also the more diffuse nonspecific inflammatory infiltration.

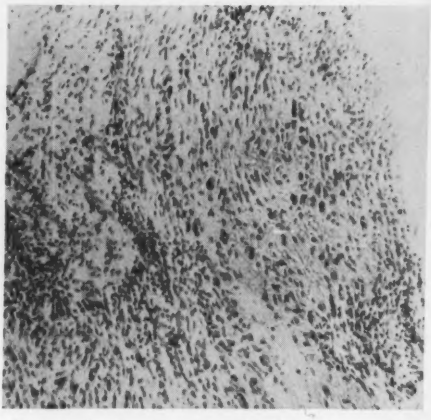


FIG. 4. Acute rheumatic valvulitis in the mitral valve. There is considerable inflammatory thickening of the valve substance. Close to the surface there are two adjoining foci of relative acellularity, fibrinoid necroses, delineated by an accumulation of large cells identical with those characterizing Aschoff nodules.

but when they are, necrotic fragmented collagen may be seen in the cores of the nodules. Similar cellular aggregates occur in the endocardium, particularly of the left atrium as MacCallum described;[11,12] here, as in lesions of the aortic media,[12] the cellular components are arranged in rows between the normally present elastic fibers. Nodular aggregates occur less commonly in the epicardium and pericardium and explain the frequency of fibrinous pericarditis. The heart valves and the inserting chordae tendineae are thickened, edematous and hyperemic with poorly circumscribed accumulations of Aschoff cells about foci of collagenous necrosis as well as more diffuse nonspecific inflammation. Characteristically an area of fibrinoid necrosis underlies the verrucae found at the margin of closure of the valves. (Fig. 4)

The valves of the left heart are far more commonly involved than those of the right. Mitral disease is most common, followed by combined mitral and aortic and then by aortic valvulitis. In the heart, the characteristic cell of the Aschoff nodule is derived from the Anitschkow cell recognizable by the characteristic central bar of nuclear chromatin, a

cardiac histiocyte and not the muscle forming cell it was originally thought to be.[14] Hyperplasia of Anitschkow cells, per se, however is not diagnostic of rheumatic infection since they respond to a variety of inflammatory conditions affecting the myocardium.[15] As evidence of a widespread affliction of collagen, focal fibrinoid degeneration occurs frequently in synovia, tendinous tissue and subcutaneous tissue inducing in each instance a palisading histiocytic reaction as well as a more diffuse exudative and nonspecific infiltration. In about 15 per cent of cases focal inflammatory and degenerative lesions of muscular arteries are found.[16] Although no specific information is available regarding the durability of the Aschoff body, after the disease has persisted three to six months many of the nodules show reduced cellularity and shrinkage and elongation of the individual cells along the progressively thickening collagenous fibers which traverse them. (Fig. 3) There is no longer evidence of collagen necrosis; the ultimate result is a fusiform acellular scar closely applied to the adventitia of a small artery.[17] With subsidence of the acute rheumatic episode there is also variable scarring of the afflicted valves whose extent and progression largely determine the subsequent clinical course.

TABLE 1

RHEUMATIC FEVER OBSERVED FOR 20 YEARS, 1000 PATIENTS, ADAPTED FROM BLAND & JONES, 1951[17]

	Potential Rheumatic H. D.	Rheumatic H. D.	Dead
Original Status (average age 8 years)	347	653	—
	76	83*	
Ten Years Later	323	475	202
	32	71*	
Twenty Years Later	319	380	301

* ¾ without recurrence of acute rheumatic fever.

TABLE 2

INCIDENCE OF ASCHOFF BODIES IN ATRIAL APPENDAGES

Removed during valvulotomy for mitral stenosis

	Case Incidence	Per cent
Pinninger (1951)	10/15	67
Waaler (1952)	8/28	28
Kuschner et al. (1952)	4/11	36
Sabiston & Follis (1952)	32/43	74
Biörck et al. (1952)	8/18	44
Janton et al. (1952)	14/88	16
Kuschner et al. (1953)	14/28	50
Enticknap (1953)	29/71	41
Decker et al. (1953)	83/183	45
Thomas et al. (1953)	22/40	55
McKeown (1953)	24/53	45
Denst et al. (1954)	21/75	28
Luse et al. (1954)	32/77	42
Elster et al. (1954)	9/15	60
Manchester et al. (1955)	13/55	37
Tedeschi et al. (1955)	75/400	19
	398/1180	33

Several studies have shown that the initial attack leaves about two-thirds of its young victims with clinically recognizable valvular heart disease. Although these are permanent structural changes, body growth and development evidently reduce their relative importance so that over the course of 20 years, Bland and Jones, 1951,[18] noted the loss of clinically detectable valvular disease in approximately one-sixth of his subjects. Simultaneously, however, this fortunate development is more than offset by the appearance of discernible heart disease in about one-fourth of those who initially escaped. (Table 1) Aschoff nodules observed in auricular appendage biopsies[19] indicate continued activity of the rheumatic process in one-third of cases despite the regular absence of all other clinical and laboratory evidence. (Table 2) (Fig. 2) While this does explain the progressive development of valvular disease in the post-rheumatic state, there is obviously a need for some clinical method of determining the presence or absence of smoldering disease.

TABLE 3

RHEUMATIC VALVULAR DISEASE, 779 SUBJECTS, ADAPTED FROM CLAWSON, 1940

Type	A	M	AM	AMT	AMTP	MT	OTHER	
Acute	2	43	24	10	9	9	1 P	
Recurrent	2	21	30	11	4	6	1 AT	1 AMP
Valve Deform.								
Incompl. Healed	4	65	28	8	1	7		
Healed	17	149	45	17	0	9	1 P	
Calc. nod aortic	136	0	92	5	0	0	1 AT	
Adher. pericard.	6	11	2	1	0	0		
Total	167	289	221	52	14	31	4	1

A —Aortic
M —Mitral
AM—Aortic, Mitral
AMT —Aortic, Mitral, Tricuspid
AMTP—Aortic, Mitral, Tricuspid, Pulmonic
MT —Mitral, Tricuspid

In chronic rheumatic heart disease there are deformities of mitral or aortic valves and hypertrophy and dilatation resulting from their chronic dysfunction. Heart failure is by far the greatest cause of death from rheumatic heart disease, 80 per cent in Bland and Jones' study; of the remainder, bacterial endocarditis was responsible for 10 per cent and assorted causes for 10 per cent.[18] There may be involvement of the valves of the right heart in addition to those of the left with severe disease; but rheumatic disease limited to the right heart is exceedingly rare. With recurrent rheumatic episodes involvement of the tricuspid and pulmonic valves are more frequent presumably related to the increased pressure in the pulmonary circulation.[20] As Bland and Jones have shown clinically, the end result of rheumatic mitral valvulitis is stenosis; progressively more of it appears with survival beyond the original episode. This may come about without clinical recurrent disease as well as with it and again stresses the importance of the subclinical activity revealed by auricular biopsies. The scarred mitral valve has thickened fused leaflets and shortened thickened chordae tendineae which interfere with their motility; (Fig. 5) with insufficiency, valvular apposition is faulty. With chronicity, further scarring occurs sometimes with focal nodular deposits of calcium so that the valve leaflets become quite rigid and, since they are fused, form an A-V diaphragm with a fish-mouth like aperture. (Fig. 6) It is common to observe superficial thrombi attached to the auricular surface of the valve presumably a result of eddies in the hindered passage of blood; these may be a source of emboli,[21] or serve as a nidus which, when infected, results in bacterial endocarditis, but more significantly their organization contributes to further thickening and narrowing of the already small A-V channel. Chronic rheu-

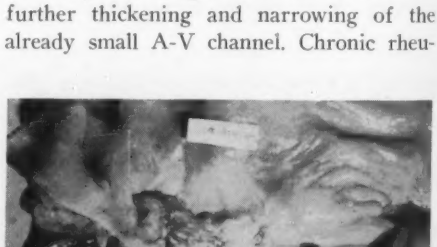


FIG. 5. Chronic rheumatic mitral valvulitis. The fused thickened valve leaflets are further distorted by nodular deposits of calcium and superficial accumulations of fibrin. The chordae tendineae are thickened and shortened. Observe also the large size of the left atrial chamber.

FIG. 6. Typical "fish mouth" deformity of chronic rheumatic mitral stenosis. This is the same valve depicted in figure 5, visualized from the enormous left atrial chamber above.

matic disease of the aortic valve results in fibrous thickening of the cusps and adhesions bridging the commissures between them. It is evident that with impaired motility there will be interference with both opening and closure. Progressive scarring and valvular fusion eventuates in a stenotic rigid aortic orifice to which curling and retraction of the cusp margins contributes a variable degree of insufficiency. Nodular deposits of calcium frequently occur in the thickened valve cusps and commissures and for this reason the term calcific or calcareous aortic stenosis has been recommended. Although some authorities contend that virtually all such lesions are rheumatic in origin and there is no doubt that rheumatic infection can produce them; when it is the sole valve involved, other causes must be considered. In this regard the infrequency of acute or subsiding aortic valvulitis contrasts with the frequency of chronic aortic disease in Clawson's tabulation.[22] (Table 3)

One last word about chronic rheumatic heart disease seems warranted. Quite frequently the pathologist finds no evidence of Aschoff bodies which would stigmatize the lesion. All the other changes in valves, myocardium and vessels are nonspecific and there is a pitfall in making an etiologic diagnosis based upon them. Although rheumatic fever most certainly is the commonest cause of the valvular lesions depicted, it would be foolhardy to deny that other processes, even though rare, may produce identical changes. For example, Saphir has demonstrated remarkable similarity between the valvular lesions of chronic erysipelothrix rhusopathiae in the pig and those of chronic rheumatic heart disease.[23] Accordingly, the medical history and record of the patient are as essential to an accurate pathologic diagnosis as they are to sound medical judgment and care.

There are excellent clinical and epidemiological grounds for relating rheumatic fever to nasopharyngeal infections with hemolytic Lancefield A streptococci. Historically, acute tonsillitis and scarlet fever have often been observed to precede attacks of acute rheumatic fever[24] by an interval of two to three weeks. Virtual epidemics in the service training camps during World War II led to the creation of the *Streptococcal Disease Commission* whose studies confirmed this finding; demonstrated the absence of rheumatic fever following other types of bacterial or even streptococcal infection; showed that the acute rheumatic state was associated with an immunologic response to antigenic components of the group A streptococci; and showed the efficacy of antibiotics in reducing the frequency of Strep A infections and recurrent acute episodes in known rheumatic subjects. [25, 26, 27]

Lancefield established 11 groups of hemolytic streptococci on the basis of immunologic differences between carbohydrate (C) fractions isolated from their cell bodies.[28] For humans, streptococci of Group A are by far the most important, and are the only ones that have rheumatogenic properties. A large

number of cell types may be identified by specific antigenic components of the bacterial cell, M protein and T substance; nucleoprotein fractions, or P substance, lack specificity. Soluble antigenic substances elaborated by the organism are of more immediate importance since a readily measurable antibody response follows more than 80 per cent of Strep A infections.[29, 30, 31] Determination of rising antistreptolysin O titers, accordingly helps to identify the etiology of an infection which in about 10 per cent of cases is succeeded by rheumatic fever or causes recurrent rheumatic fever in 25 to 50 per cent of established rheumatic heart disease.[29] The changes in antifibrinolysin and antihyaluronidase parallel those of antistreptolysin. No correlation exists between the hylauronidase productivity of the infecting streptococcus and its rheumatogenic properties,[29] contrary to earlier suggestions. Several studies[30] however have indicated a slight delay of the immunologic response to the rheumatic post streptococcal state as compared with the nonrheumatic group.

The pathogenesis of the cardiac and other changes are not definitely established. Since Klinge (1933)[32] produced foci of fibrinoid degeneration and since Rich and Gregory (1943)[33] also induced focal cellular aggregates in cardiac muscle and valves by anaphylactic hypersensitivity, it has been proposed that the rheumatic lesion in the human represents a hypersensitivity reaction to hemolytic streptococci or their products. Murphy and Swift[34] were even more successful in mimicking the rheumatic lesions of humans by repeated subcutaneous Strep A infections in rabbits; their experiments moreover were without the diffuse arteritis and glomerulitis which characterized Rich and Gregory's[33]work. Nonetheless the problem remains unsolved. Kaplan[35] has shown that the streptococcal preparation used by Murphy and Swift carried sufficient beef heart antigen (from the bacteriologic media) to induce the formation of antibodies reactive with normal rabbit heart. This sequence did not occur if a synthetic medium were substituted.

It is only of historic interest to mention the other views that have been entertained but discarded for lack of substantiation. These include: streptococcal viridans infection,[36] a presumed virus,[37] and deficiency of vitamin C.[38] The clinical evidence linking streptococcal A infections with rheumatic fever is overwhelming and outweighs the gaps in our knowledge of its pathogenesis.

References

[1] White, P. D.: Heart Disease, ed. 4, 1051 pp. Macmillan, New York, 1951.

[2] Paul, J. R.: The epidemiology of rheumatic fever. In Piersol, G. M. and Mortz, E. L.: The Cyclopedia of Medicine, Surgery and Specialities. Phila., Davis, vol. 3, pp. 629-633, 1945.

[3] Pitcairn, D.: Cited from Baillie, M. The Morbid Anatomy of Some of the Most Important Parts of the Human Body. 3rd American ed., p. 30, Phila., 1820.

[4] MacLagan, T. J.: Rheumatism: its nature, its pathology and its successful treatment. London, Pickering, 333 pp.

[5] Goodhart, J. F.: Case of rapid enlargement of the heart. Tr. Path. Soc., London, 30:279, 1879.

[6] Aschoff, L.: Zur Myocarditisfrage, Verhandl. d. deutsch. path. Gesellsch., 8 meeting 2nd part, p. 46-53, 1904.

[7] Von Glahn, W. C. and Pappenheimer, A. M.: Specific lesions of peripheral blood vessels in rheumatism. Am. J. Path., 2:235-250, 1926.

[7] Von Glahn, W. C. and Pappenheimer, A.M.: Specific lesions of peripheral blood vessels in rheumatism. Am. J. Path., 2:235-250, 1926.

[8] Talalajew, W. T.: Der akute Rheumatismus, Klin. Wchnschr. 8:124-129, 1929.

[9] Klinge, F., and Vaubel, E.: IV. Mitteilung. Die Gefässe beim Rheumatismus; insbesondere die "Aortitis rheumatica." Virchows Arch. f. path. Anat. 281:701-747, 1931.

[10] Altschuler, C. H., and Angevine, D. M.: Histochemical studies on the pathogenesis of fibrinoid. Am. J. Path. 25:1061-1076, 1949.

[11] MacCallum, W. C.: Rheumatic lesions of the left auricle of the heart. Bull. Johns Hopkins Hosp. 35:329, 1924.

[12] Von Glahn, W. C.: Auricular endocarditis of rheumatic origin. Am. J. Path. 2:1-14, 1926.

[13] Pappenheimer, A. M., and von Glahn, W. C.: Lesions of the aorta associated with acute rheumatic fever, and with chronic cardiac disease of rheumatic origin. J. M. Research, 44:489-506, 1924.

[16] Ehrlich, J. C., and Lapan, B.: The Anitschkow "myocyte." Arch. Path., 28:361-370, 1939.

[17] Clawson, B. J.: Relation of "Anitschkow myocyte" to rheumatic inflammation. Arch. Path., 32: 760-763, 1941.

[18] Gross, L., Kugel, M. A., and Epstein, E. Z.: Lesions of the coronary arteries and their branches in rheumatic fever. Am. J. Path. 11:253-280, 1935.

[17] Gross, L. and Ehrlich, J. C.: Studies of the myocardial Aschoff body. Am. J. Path. 10:467-488, 1934.

[18] Bland, E. T., and Jones, T. D.: Rheumatic fever and rheumatic heart disease; 20 year report on 1000 patients followed since childhood. Circulation 4:836-843, 1951.

[19] Tedeschi, C. G., Wagner, B. M., and Pani, K. C.: Studies in rheumatic fever. 1. The clinical significance of the Aschoff body based on morphologic observations. Arch. Path., 60:408-422, 1955.

[20] Baggenstoss, A. H.: Rheumatic disease of the heart. Chapt 8, Pathology of the Heart, S. E. Gould, edit. pp. 1023, Charles C Thomas, Springfield, Ill., 1953.

[21] Angrist, A. A., and Marquiss, J.: Changing morphologic picture of endocarditis at necropsy since the advent of chemotherapy and antibiotic agents. Am. J. Path., 29:594, 1953.

[22] Clawson, B. J.: Rheumatic heart disease; analysis of 796 cases. Am. Heart J., 20: 454-475, 1940.

[23] Saphir, O., and Lowenthal, M.: Old endocarditis in the hearts of pigs resembling human endocarditis. Am. J. Path. 25:824, 1949.

[24] Glover, J. A.: Milroy lectures on the incidence of rheumatic diseases; the incidence of acute rheumatism. Lancet 1:499-505, 1930.

[25] Rantz, L. A., Boisvert, P. J., and Spink, W. W.: The etiology and pathogenesis of rheumatic fever. Arch. Int. Med. 76:131, 1945.

[26] Rantz, L. A.: The natural history of hemolytic streptococcus sore throat. California Med., 65:266, 1946.

[27] Rantz, L. A., Randall, E., and Rantz, H. H.: Immunization of human beings with group A Hemolytic streptococci. Am. J. Med., 6:424-432, 1949.

[28] Lancefield, R. C.: Specific relationship of cell composition to biological activity of hemolytic streptococci. Harvey Lectures 1940-41. Baltimore, 1941, Williams and Wilkins Co.

[29] Swift, H. F.: Relationship of streptococcal infections to rheumatic fever. Am. J. Med. 2:168-189, 1947.

[30] Rothbard, S., Watson, R. F., Swift, H. F. and Wilson, T. T.: Bacteriologic and immunologic studies on patients with hemolytic streptococci infecttions as related to rheumatic fever, Arch. Int. Med. 82:229-250, 1948.

[31] Houser, H. B., and Eckhardt, G. C.: Recent developments in prevention of rheumatic fever. Ann. Int. Med., 37:1035-1043, 1952.

[32] Klinge, F.: Der Rheumatismus, Ergeben. d. allg. Path. u. path. Anat., 27:1-354, 1933.

[33] Rich, A. R., and Gregory, J. E.: Experimental evidence that lesions with the basic characteristics of rheumatic carditis can result from anaphylactic hypersensitivity. Bull. Johns Hopkins Hosp.; 73: 239-264, 1943.

[34] Murphy, J. E., and Swift, H. F.: The induction of rheumatic-like cardiac lesions in rabbits by repeated focal infections with Group A Streptococci. J. Exp. Med. 91:485-498, 1950.

[35] Kaplan, M. H.: Production of autoimmune bodies to heart tissue in rabbits inoculated with streptococcal cultures; nature and histologic localization of the reactive antigen. Fed. Proc., 15, Part 1:596, 1956 (#1942).

[36] Swift, H. F.: The pathogenesis of rheumatic fever. J. Exp. Med. 39:497-508, 1924.

[37] Schlesinger, B., Signy, A. G., and Amies, C. R.: Etiology of acute rheumatism; experimental evidence of a virus as the causative agent. Lancet, 1:1145-1146, 1935.

[38] Rinehart, J. F.: Studies relating vitamin C deficiency to rheumatic fever and rheumatoid arthritis; experimental, clinical and general considerations. I. Rheumatic fever. Ann. Int. Med., 9:586-599, 1935.

Clinical Aspects of Coronary Arteriosclerosis*

By

COLONEL BYRON E. POLLOCK, MC, *U. S. Army*†

THE pathology embraced by the term "coronary arteriosclerosis" includes: (a) coronary atherosclerosis, responsible for the great majority of cases of clinical coronary artery disease, and (b) medial coronary sclerosis of infancy,[1] also known as medial calcification with fibroblastic proliferation of the intima.[2,3]

MEDICAL CORONARY SCLEROSIS OF INFANCY

Stryker[3] has reported 5 cases of medial coronary sclerosis and collected 15 cases from the literature. This condition occurs in infants, reported at ages of 1 day to 7 months. In 5 cases the infant died suddenly without known clinical symptoms, while others showed varying clinical evidence of cardiac failure, upper respiratory symptoms, recurrent elevation of temperature, and difficulty in feeding. In a case of Brown and Richter,[1] a boy of 3½ months age, apparently in good health, suddenly became dyspneic and cyanotic and vomited once. Respiration and heart rate became very rapid. After two short tonic convulsions, the child died less than 24 hours following the onset.

The cause of medial coronary sclerosis remains unknown; no factor common to all cases has been found. An alteration of calcium and phosphorus metabolism is suspected due to association in some of the cases with heavy vitamin D administration, severe associated renal lesions, or maternal hyperparathyroidism. Stryker postulates the action of diet, infection, and other factors acting on a congenitally weak protoplasm.

From the clinical point of view, medial coronary sclerosis of infancy is a rare condition offering few diagnostic clues to the physician. So far as I am aware ante mortem diagnosis has not been made.

CORONARY ATHEROSCLEROSIS

Coronary atherosclerosis produces clinical manifestations of several types depending upon circumstances in individual cases. The manifestations of angina pectoris, intermediate coronary syndrome, myocardial infarction, silent cardiac enlargement and hypertrophy, congestive heart failure, heart block and cardiac arrhythmias are produced.

Angina Pectoris. The original clinical description of angina pectoris was given by Heberden in a lecture before the Royal College of Physicians in London in 1768 and first published in 1772.[4] The exellence of this description justifies verbatim quotes from it: "—there is a disorder of the breast marked with strong and peculiar symptoms, considerable for the kind of danger belonging to it, and not extremely rare, which deserves to be mentioned more at length. The seat of it, and sense of strangling with which it is attended, may make it not improperly be called angina pectoris."

"Those who are afflicted by it, are seized while they are walking (more especially if it be uphill, and soon after eating) with a painful and most disagreeable sensation in the breast, which seems as if it would extinguish life, if it were to increase or to continue; but the moment they stand still, all this uneasiness vanishes.

"In all other respects, the patients are, at the beginning of the disorder, perfectly well, and in particular have no shortness of breath, from which it is totally different. The pain is sometimes situated in the upper part, sometimes in the middle, sometimes at the bottom of the os sterni, and often more inclined to the left than to the right side. It likewise very frequently extends from the breast to the middle of the left arm. The pulse is, at least sometimes, not disturbed by this pain, as I have had opportunities of observing by feeling the pulse during the

* Presented at the Post Graduate Seminar on Diseases of the Heart, Armed Forces Institute of Pathology, Washington, D.C., May 14-17, 1956.

† Cardiology Service, Fitzsimons Army Hospital, Denver, Colo.

paroxysm. Males are most liable to this disease, especially such as have past their fiftieth year."

". . .

". . . the access and the recess of the fit is sudden. . . . Wine and spiritous liquors, and opium afford considerable relief. . . . It is increased by disturbance of the mind. . . . Its attacks are often after the first sleep. . . ."

Since the time of Heberden, little has been added to the clinical description of angina pectoris. Significant advances have been discovery of immediate action of nitrites such as amyl nitrite[5] and nitroglycerin[6] in relief of the acute attack, and the effect of longer acting drugs such as pentaerythritol tetranitrate (Peritrate®)[7] in preventing attacks or reducing their frequency. Electrocardiographic studies have sometimes shown transient changes consisting of depression of RS-T segments or inversion of T waves during the acute attack of angina pectoris. Tests based on producing these changes by exercise[8] and by the breathing of oxygen poor gases[9] have been devised.

Myocardial Infarction. As Herrick[10] pointed out in his original description of clinical features of sudden obstruction of the coronary arteries, the symptoms of myocardial infarction are quite variable, extending from sudden, seemingly instantaneous death, to attacks of severe anginal pain with profound shock, to milder attacks of long continued substernal pain, anginal in character, usually appearing without exertion, and not relieved by nitrites. We now know that milder symptoms may be present in some cases of infarction, such as weakness, fatigue, and apprehension, with little or no pain in the precordium.

The pain of myocardial infarction is usually substernal in location, and may radiate to the neck, lower jaw, and one or both shoulders or arms. A sensation of flatulence and indigestion may lead the patient to blame the stomach for his discomfort. A fear of death frequently accompanies the attack. A sense of strangling is sometimes present, but unassociated with any real shortness of breath or respiratory obstruction.

The electrocardiogram frequently reveals evidence of current of injury, myocardial ischemia and later, tissue necrosis. The electrocardiographic lead taken over an area of infarction shows early elevation of the RS-T segment, with later inversion of the terminal portion of the T wave. An increase in depth and width of the Q wave develops, often with reduction in the height of the R wave. An ECG lead taken over uninjured myocardium sometimes shows early reciprocal changes of depression of the RS-T segment, terminal uprightness of the T wave. With the passage of days, the RS-T segment changes disappear while T wave inversions become more prominent. In a matter of weeks, the T wave may become less deep, and in a matter of weeks to months, the T wave may return to the isoelectric line or above. A prominent Q wave may return to normal appearance but more often remains to signal the location of the old infarction. By a study of electrocardiographic leads taken over several areas of the chest and limbs, one can locate the area of myocardial infarction anatomically with reasonable accuracy.

The systemic reaction to death of myocardial tissue consists of fever, leucocytosis and elevation of the erythrocyte sedimentation rate. Fever is usually of low grade and appears in about 24 hours, disappears in a few days. Leucocytosis is of moderate degree, appears within a few days and is usually gone within a week. Elevation of the erythrocyte sedimentation rate develops and recedes more slowly. The height and duration of these alterations correlates roughly with the extent of myocardial necrosis. Death of myocardial tissue releases into the blood glutamic oxalacetic transaminase which can be measured in the serum.[11] A significant elevation is found at 24 hours, with rapid decline to normal levels in ensuing days.

Early complications of acute myocardial infarction are sufficiently common as to confirm the diagnosis in some cases, while at the same time making treatment more complex. Shock occurs in some 10 per cent of

cases. Acute left heart failure manifested by pulmonary edema may result promptly and directly from the infarction. Cardiac arrhythmias are common, but fortunately they are non-specific and benign for the most part. Ventricular paroxysmal tachycardia is a rather specific and dangerous complication. Focal pericarditis about the infarcted area is common, producing a brief transient pericardial friction rub on the second or third day. Rarely a generalized pericarditis develops, which then serves to make the diagnosis of myocardial infarction more difficult. Congestive heart failure with the usual pulmonary and peripheral manifestations may occur either early after the infarction or later during the patient's resumption of physical activity. Pulmonary embolism may result from thrombi formed during stagnation of blood in the peripheral veins and right heart due to absolute rest or congestive failure. Arterial embolization may result from dislodgement of fragments of a mural thrombus in the left ventricle at the site of a myocardial infarction.

The Intermediate Coronary Syndrome. The observation of patients with acute coronary symptoms will reveal certain ones whose manifestations seem more prolonged than those of angina pectoris and yet do not meet the criteria for acute myocardial infarction. Blumgart and his associates[12] introduced the term "coronary failure" to include the cases with attacks of coronary pain more prolonged than those of angina pectoris, but without clinical, laboratory or post-mortem evidence of myocardial infarction. Such attacks may occur under conditions which place extra demands on the heart, such as exercise, emotion or paroxysmal heart action. In other cases a fall of blood pressure (shock) is apparently responsible. In some cases occurring at rest or under circumstances which have not previously provoked attacks, the cause may be an acute coronary occlusion without infarction.

Master and his associates[13] in 1941 discussed the occurrence of myocardial infarction without coronary occlusion, and used the term "coronary insufficiency" to designate the mechanism. They pointed out that coronary insufficiency resulted from either reduction in coronary blood flow or increase in oxygen requirements of the heart. A careful clinical study failed to reveal diagnostic differences in symptoms of infarction whether due to coronary occlusion or coronary insufficiency. The electrocardiogram, however, was apt to show evidence for subendocardial infarction, residing in depression of the RS-T segment and changes in the T wave, without elevation or the appearance of a significant Q wave, the electrocardiogram usually returns to its original configuration in several days or weeks.

In a later paper,[14] Master and his group extended the discussion of coronary insufficiency to include patients without evidence for myocardial infarction, whose manifestation might include only simple transitory chest pain, little or no fever, and no significant change in blood pressure, and little or no leucocytosis and elevation of the erythrocyte sedimentation rate. In such cases the electrocardiogram might be normal, and the patient asymptomatic but the diagnosis could be established by obtaining characteristic electrocardiographic changes after exercise.

Thus we have a clinical condition due to coronary artery disease which gives symptoms and laboratory findings lying between those of angina pectoris and myocardial infarction, designated on the anginal end of the spectrum by one group as "coronary failure" and on the infarction end of the spectrum as "coronary insufficiency." Scherf and Golbey[15] have recently decried the use of "coronary insufficiency" to suggest a diagnosis or a pathological entity rather than as a strictly physiological term.

At the risk of further confusion, Graybiel[16] has attempted to clarify the nomenclature by introducing the term "intermediate coronary syndrome" "to distinguish an acute attack due to coronary heart disease which is intermediate in severity between angina pectoris and myocardial infarction." Evaluation of the pain distinguishes it from the anginal syndrome and evaluation of the

other clinical findings distinguishes it from myocardial infarction.

The pain in the intermediate coronary syndrome is more prolonged than that of angina, particularly longer than that of previous attacks in the patient who suffers from angina. It lasts longer than a few minutes after the precipitating factor is removed, or after the administration of nitroglycerin. The character of the pain is not essentially different from that of angina. The pain may appear without obvious inciting cause, or with much less than the usual cause. The electrocardiogram does not show definite changes of either transmural or subendocardial infarction, although serial electrocardiograms may show brief transient depression of the RS-T segment and lowering or inversion of the T waves.

A systemic response to infarction is lacking. Fever does not develop, leucocytosis and elevation of the erythrocyte sedimentation rate do not occur. The serum glutamic oxalacetic transaminase level is not altered. The patient feels well after subsidence of the pain and the physical examination often reveals no significant abnormality.

The clinical course is short and usually mild, with recovery to the condition existing prior to the attack. Progression or exacerbation may lead to myocardial infarction, or intercurrent death from ventricular fibrillation may rarely occur.

Other Manifestations of Atherosclerotic Coronary Artery Disease. In patients who have no evidence for present or past myocardial infarction, coronary insufficiency, or angina pectoris the diagnosis of arteriosclerotic heart disease is always uncertain, but may be presumed on the basis of heart enlargement, congestive heart failure, heart block or chronic auricular fibrillation when no other cause for these conditions is found after an adequate study.

Cardiac enlargement is not a necessary finding in arteriosclerotic heart disease; in fact, the heart size as determined by roentgenographic studies is usually normal in cases of angina pectoris, and may either enlarge or remain normal after myocardial infarction.[17] Whenever congestive heart failure complicates infarction, cardiac enlargement almost always develops. Hypertensive patients with coronary artery disease are especially prone to cardiac enlargement. There remain, however, occasional patients over 40 years of age who develop gradually increasing heart size, usually due to left ventricular dilatation and hypertrophy, whose examination reveals no cause other than coronary atherosclerosis. In these patients, left sided heart failure or generalized congestive heart failure may result with the passing of time.

Acute left-sided heart failure manifested by attacks of paroxysmal dyspnea, especially at night, and rarely, the development of pulmonary edema, may follow myocardial infarction or the anginal syndrome, but may also develop insidiously in the patient with arteriosclerotic heart disease.

A generalized congestive heart failure may follow left-sided failure or form the presenting manifestation of arteriosclerotic heart disease. The usual symptoms of shortness of breath on exertion and ankle edema are present, with findings of fine rales over the lung bases, engorgement of the liver, peripheral edema, a general increase in venous pressure, etc.

Atrioventricular heart block may occur in arteriosclerotic heart disease. Prolongation of the P-R interval of the electrocardiogram, or partial A-V block with the occasional or regular dropping of ventricular beats is not uncommon. Complete heart block is rather rare, but coronary atherosclerosis is its commonest cause. Adams-Stokes attacks may occur in these cases.

Bundle branch block, especially of the left bundle, often signifies coronary artery disease. Patients who develop this finding often, but not always, present other evidence for arteriosclerotic heart disease.

Atrial fibrillation is a common accompaniment of several types of heart disease. Next to rheumatic heart disease, however, arteriosclerotic heart disease is its most common cause. Atrial fibrillation occurs commonly in advanced cases of arteriosclerotic heart dis-

ease with congestive heart failure. The onset of atrial fibrillation, however, may be the first evidence which leads to the discovery of previously unrecognized arteriosclerotic heart disease.

Etiological Considerations. Arteriosclerotic heart disease due to coronary atherosclerosis occurs in individuals from ten years of age upward. The incidence increases progressively with advancing years. With the increasing longevity of the population it is the dominant cause of death from heart disease. There is a decided susceptibility of the male. After the menopause this sex difference is much less. Hypertension, diabetes, obesity, familial xanthomatosis, myxedema and chronic glomerulonephritis favor the development of coronary atherosclerosis, and these diseases in the female reduce rather markedly the sex difference in incidence of arteriosclerotic heart disease. Heredity has not been thoroughly documented as a factor, but may play a role in this condition.

There is widespread suggestive evidence favoring the belief that coronary atherosclerosis is a result of a disturbance in lipoid metabolism, which special attention to cholesterol. Extensive study is being applied at this time. An increased incidence of atherosclerosis is well known in diseases associated with hypercholesterolemia, such as familial xanthomatosis, myxedema, and possibly diabetes. Dietary studies in various parts of the world have been interpreted as showing that peoples who consume a high-fat diet have a higher rate of atherosclerosis. Atherosclerosis has been produced in animals by techniques including a high-fat diet or excess cholesterol feeding; differences between reactions of different species and differences between the experimental animal lesion and the human lesion give ground for differences in opinion as to the significance of the results. Analyses of the cholesterol levels and differential plasma lipoprotein levels in humans with and without known atherosclerosis have produced suggestive but not clear cut evidence of their role in producing the human disease.

The role of hypertension in producing atherosclerosis is a major one, but is not essential to the process. Its mechanism is poorly understood.

Any satisfactory explanation of the cause of atherosclerosis must explain the preponderant involvement of the male sex; there is little definite knowledge in this field. Study of the relationship of thyroid insufficiency or pituitary and adrenal tumors to atherosclerosis is complicated by the concomitant hypercholesterolemia and in some cases hypertension also. Association with diabetes also suggests a pancreatic role in atherosclerosis which remains undefined.

Summary

The pathology embraced under the term "coronary arteriosclerosis" includes coronary atherosclerosis, responsible for the great majority of cases of clinical coronary artery disease; and medial coronary sclerosis of infancy, also known as medical calcification with fibrolastic proliferation of the intima.

Stryker has reported 5 cases of medial coronary sclerosis and collected 15 cases from the literature. This condition occurs in infants from 1 day to 7 months of age. In 5 cases the infant died suddenly without known clinical symptoms, while others showed varying clinical evidence of cardiac failure, upper respiratory infection, recurrent elevation of temperature, difficulty in feeding.

Coronary atherosclerosis produces clinical manifestations of several types depending on circumstances in individual cases. The manifestations of angina pectoris, intermediate coronary syndrome, myocardial infarction, silent cardiac hypertrophy, and congestive heart failure are produced.

Angina pectoris (of Heberden) is manifested typically by brief attacks of substernal pain produced by physical or emotional stress, relieved by rest and nitroglycerin. The pain may radiate to the neck, jaws, shoulders and arms.

Myocardial infarction may produce sudden symptoms similar to those of angina

pectoris with or without exertion or mental stress. The pain is long persisting, not relieved by nitrites, and accompanied by much apprehension. Usually electrocardiographic changes of typical character occur, and elevations for a period are noted in the body temperature, the leucocyte count and the erythrocyte sedimentation rate. Complications of shock, pulmonary edema, arrhythmias and congestive heart failure are not uncommon.

A number of cases of the coronary syndrome fit clinically between the typical picture of angina pectoris and myocardial infarction. The pain is more prolonged than that of angina pectoris. Transient electrocardiographic changes may occur, but fever, leucocytosis, and elevation of the erythrocyte sedimentation rate do not appear. Such cases may progress into myocardial infarction or resolve more or less completely. The terms "coronary failure," "coronary insufficiency" and "intermediate coronary syndrome" have been applied to this condition.

In some individuals, a gradual progressive cardiac enlargement with evidence electrocardiographically of left ventricular hypertrophy occurs. Although several etiologic causes for this sequence may be possible, in a large proportion of such cases no cause other than coronary atherosclerosis may be found. Congestive failure manifested by paroxysmal nocturnal dyspnea, or more generally with manifestations of shortness of breath, engorgement of the liver and ankle edema may follow.

Cardiac conduction defects such as atrioventricular block and bundle branch block may occur in patients with coronary atherosclerosis. Auricular fibrillation is not uncommon.

Etiological considerations include the role of dietary fat and cholesterol, the place of abnormal endogenous lipid metabolism, influence of sex and endocrine glands, and the mechanism of hypertension in the production of atherosclerotic coronary lesions. Much investigation is being conducted, but definite knowledge of the etiology and mechanisms involved is not now available.

References

[1] Brown, C. E. and Richter, I. M.: Medial Coronary Sclerosis in Infancy. Arch. Path. 31:449-457, Apr. 1951.

[2] Stryker, W. A.: Coronary Occlusive Disease in Infants and Children. Am. J. Dis. Child. 71:280-300, Mar. 1946.

[3] Stryker, W. A.: Arterial Calcification in Infancy with Special Reference to the Coronary Arteries. Am. J. Path. 22:1007-1031, Sept. 1946.

[4] Heberden, W.: Commentaries on the History and Cure of Diseases, London, 1802. From Willius, F. A. and Keys, T. E.: Cardiac Classics. St. Louis, The C. V. Mosby Company, 1941, pp. 222-224.

[5] Brunton, T. L.: On the Use of Nitrite of Amyl in Angina Pectoris. Lancet 2: 97-98, 1867.

[6] Murrell, W.: Nitro-glycerin as a Remedy for Angina Pectoris. Lancet 1:80-81; 113-115; 151-152; 225-227, 1879.

[7] Bjerlov, H.: Paper read at St. Mary's Hospital, Stockholm, 1942, Svenska Lak T. 40:694, 1943, cited by Weitzman, D.: Penta-Erythritol Tetranitrate in Treatment of Angina. Brit. M. J. 2:1409-1412, 26 Dec. 1953.

[8] Master, A. M.: The Two-Step Test of Myocardial Function. Am. Heart J. 10:495-510, April 1935.

[9] Levy, R. L., Bruenn, H. G. and Russell, N. G., Jr.: The Use of Electrocardiographic Changes Caused by Induced Anoxemia as a Test for Coronary Insufficiency. Am. J. M. Sc. 197:241-247, Feb. 1939.

[10] Herrick, James B.: Clinical Features of Sudden Obstruction of the Coronary Arteries. J.A.M.A. 59: 2015-2020, Dec. 7, 1912.

[11] La Due, J. S. and Wroblewski, F.: The Significance of Serum Glutamic Oxalacetic Transaminase Activity Following Acute Myocardial Infarction. Circulation 11:871-887, June 1955.

[12] Blumgart, H. L., Schlesinger, M. J., and Zoll, P. M.: Angina Pectoris, Coronary Failure and Myocardial Infarction; Role of Coronary Occlusions and Collateral Circulation. J.A.M.A. 116: 91-97, Jan. 11, 1941.

[13] Master, A. M., Gubner, R. Dack, S. and Jaffe, H. L.: Differentiation of Acute Coronary Insufficiency with Myocardial Infarction from Coronary Occlusion. Arch. Int. Med. 67:647-657, Mar. 1941.

[14] Master, A. M., Dack, S., Field, L. E. and Horn, H.: Diagnosis and Treatment of Acute Coronary Diseases. J.A.M.A. 141:887-891, 26 Nov. 1949.

[15] Scherf, D. and Golbey, M.: Critique: An Evaluation of Term "Coronary Insufficiency." Am. Heart J. 47:928-934, June 1954.

[16] Graybiel, A.: The Intermediate Coronary Syndrome. U. S. Armed Forces M. J. 6: 1-7, Jan. 1955.

[17] Bartels, E. C. and Smith, H. L.: Gross Cardiac Hypertrophy in Myocardial Infarction. Am. J. M. Sc. 184: 452-455, Oct. 1932.

Surgical Aspects of Coronary Arteriosclerotic Heart Disease*

By

MORRIS H. O'DELL, M.D.

Thoracic Surgeon, Charleston General Hospital, Charleston, West Virginia

(With 4 illustrations)

THE surgical treatment of coronary heart disease is quite a controversial subject. Whenever two or more physicians meet to discuss this problem, usually the opinions are quite varied. Last week (May 10, 1956) I attended the meeting of the American Association for Thoracic Surgeons hoping to obtain some unpublished late information on this subject, as well as to hear a lively discussion; but, of 43 papers presented, not a single paper dealt with coronary heart surgery. To properly cover the field of coronary heart surgery, it is necessary to delve into the history.

In the last 25 years a tremendous amount of research work has been performed to find a new blood supply for the myocardium. Almost every physician who has had facilities for research has attempted to find a way to alleviate the pain and lessen the mortality from this disease. I have not tried to cover the history completely but to give the impression that a tremendous amount of work has been done, leaving one big question—what is the best treatment of this disease surgically? Most of this effort has been performed along several lines: either to bring some structure to the heart and attach this structure to the heart to cause a growing of blood vessels into the myocardium, or to use some chemical for irritating the surface of the heart, or to create a vascular shunt between some nearby blood vessel and the coronary sinus, or to partially occlude the coronary sinus causing a back flow into the myocardium. Any combination of these methods may be used.

The first suggested method for treating coronary heart surgery was in 1899 when it was advised that nerves be resected to relieve the anginal pain. This was not performed, however, until 1916.[1] At the present time, Dr. Evans and Dr. Popin have had fairly good results with this procedure. They state it is best confined to the individual with severe angina and hypertension, and to the normotensive patient with an over-alarm syndrome.[2] Results in the latter group are not too good. The procedure to obtain the best results requires resecting the upper four thoracic ganglia on both sides, which of course includes the stellate, and means that the patient will have a bilateral Horner's syndrome. In 1932 Beck received credit for use of the first pericardial irritant to the surface of the heart to cause increased vascularity. In 1932, Blumgart advised thyroidectomy to lower the metabolism. This operation was first performed at Peter Bent Brigham Hospital on December 14, 1932.[3] It is no longer used. Others have used an omental graft, or pectoralis muscle graft, or various different combinations which I will not mention now. In 1937 Gross and his associates partially or completely ligated the coronary sinus to cause a back flow in the myocardium. Their mortality was in the range of 42% and the procedure was abandoned.[4]

In 1940 Thompson started his work using talc in the pericardium, and the method has built up quite a large number of cases since that time. In 1941 Beck and his associates repeated the work of Gross on the coronary sinus with a partial ligation and managed to reduce experimentally the mortality to 2%.[5] In 1943, Roberts was the first to use an arterial connection from nearby vascular struc-

* Presented at the Post-Graduate Seminar on Diseases of the Heart. Held at the Armed Forces Institute of Pathology, Washington, D.C., May 14-17, 1956, and Co-sponsored by The American Heart Association, Inc.

tures to the coronary sinus by means of a cannula.[6]

Beck and associates, in 1943, evaluated all of the irritants that had been used, as well as many more, experimentally to find out which chemicals caused irritation to the heart, which caused a good vascularity, and which ones would cause scar tissue formation. From his experiments, he concluded that asbestos caused the best vascular response, and that the proper amount to use was 2/10 of a gram of a coarse asbestos.[7]

In 1946 Vineberg started his work with the internal mammary artery, transplanting the left internal mammary deep into the left myocardium near the apex, leaving one branch, usually the sixth intercostal, free to bleed into the heart muscle.[8] Beck, in 1946, started his work with his II procedure using a vascular graft between the coronary sinus and the aorta. The first successful case was in 1948. Others have used a pedicled skin graft, phenol to the pericardium, and recently in the literature, Goldman has experimentally used an arterial U graft connecting the left ventricle with the left myocardium. In the non-surgical field, medical pioneers in the use of radioactive iodine are Blumgart and Jaffe, both starting their work in 1947 and publishing their results in 1952.

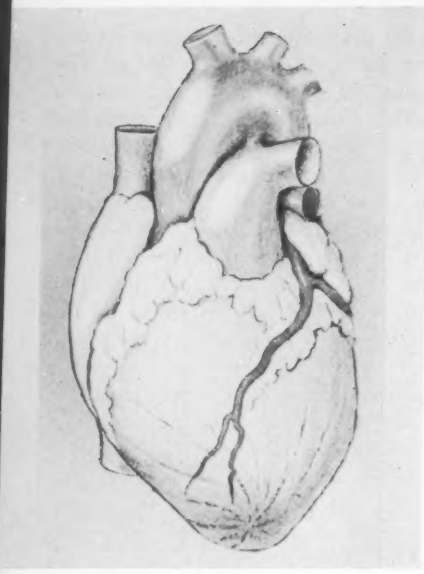
Most of this discussion has dealt with experimental work and investigation but, from experiments, the investigators have gone to actual surgical treatment of cardiac patients. For an operation to be successful it must have been used experimentally to prove it will work; it must have been used in a large number of cases; the mortality must be low; the results must be quite good. It also should be within the ability of the average surgeon to perform. When all of these results are evaluated, we then have three operations that have been used to date in a large number of cases by a large number of surgeons. These are called the Beck I, the Vineberg, and the Thompson procedures (Fig. 1).

In the Beck procedure, the outstanding part of the operation is the partial ligation of the coronary sinus. In addition, the undersurface of the pericardium is abraded. The epicardium is abraded or the lining removed so that the heart will become adherent to the adjacent fat and structure. The anterior mediastinal fat pad is gently and carefully freed. This structure has a very rich blood supply and in some patients it is quite long. This fat pad is brought under the left phrenic nerve and vessels. If long enough, it is sutured to the left border of the pericardium or, if not, directly to the left myocardium. In addition, asbestos is placed on the surface of the heart before the fat pad is brought over. The operation is performed similarly by the author except that talc is used instead of asbestos. Vineberg has as the main part of his operation, transplantation of the left internal mammary artery. In addition, the epicardium over the left ventricle is abraded and the mediastinal fat is carefully brought over to the myocardium. In the earlier procedures this fat pad was not used. Earlier the Vineberg operation consisted of transplanting the internal mammary deep into the left myocardium near the apex and avoided bringing the fat pad over the artery for fear it might cause a stricture of the artery. I have added these other two procedures: abrading the pericardium, and placing a very small amount of talc in the pericardium on the surface of the heart before the fat pad is brought over to the myocardium.

Thompson and associates use only talc. It is a very simple procedure and a very good one, and the results reported by Thompson and other surgeons are good but I personally feel that this is not quite enough. When the chest is opened it is very easy to proceed and do some of these other minor procedures such as abrading the epicardium and the pericardium. I feel that by doing a little more the patient probably has a little more longevity and perhaps a chance to work a little longer or harder without his anginal pain.

The results of the various surgeons' procedures are similar. The complete number of patients operated by the various surgeons is not given, only those patients that have suffi-

REVASCULARIZATION



BECK—I
ABRASION PERICARDIUM
ABRASION EPICARDIUM
LIGATION CORONARY SINUS TO 3 MM.
0.2 GM. ASBESTOS
MEDIASTINAL FAT TO LEFT MYOCARDIUM

VINEBERG—MODIFIED
INTERNAL MAMMARY TRANSPLANT
ABRASION PERICARDIUM
ABRASION EPICARDIUM
MEDIASTINAL FAT TO LEFT MYOCARDIUM
(TALC IN PERICARDIUM)

THOMPSON
TALC IN PERICARDIUM

FIG. 1

cient time elapse in order that they can be properly evaluated. The evaluation is a little difficult comparing each procedure with the next as each one of these surgeons has a slightly different method of evaluating his patients. In the Beck I procedure, of 103 patients 45% have no angina and 45% have less angina giving a total of 90% with improvement; 34% of these have no work limitation, 55% have work limitation. There was a 6.6% operative mortality which includes the early postoperative period and, with the 1st and 2nd year added on, gives a total of 18% mortality in the first two years. Compare this with a series of 88 patients treated medically with a two year mortality of 30%.[9] I do not include the Beck II as one of the approved operations. The Beck II operation is a very good operation and the results are quite good when it is successful. It is a highly skilled procedure. It requires, in addition to a highly skilled surgeon, a good first assistant to help the surgeon and one is not always available in smaller hospitals. There are more contraindications and less indications for the procedure. The upper age level for operation is much lower and the mortality runs considerably higher. Results reported are not any better than those of some of the simpler, less hazardous procedures. In the Beck II procedure on 44 patients there was a total of 90% improvement with 10% of this 90% showing only fair improvement. The mortality on these patients was 22%.[10] In 40 patients having the Vineberg procedure, 57% had no angina or only slight angina while 77% were able to return to work. Vineberg's mortality was 6.6% operative if he excluded patients with angina at rest.[11] Much earlier he operated on these status anginosis patients and discovered that the mortality was around 50%. Of the first 57 patients with the Thompson procedure 90% improved more than 50%, while 40% of the patients were improved more than 75%.[12] His operating mortality on these patients was 12%. This is much lower now.

Briefly, the indications for the use of radioactive iodine and the results are given. In 1954 Blumgart summarized the results from 50 clinics covering 1070 patients.[13] In addition, many articles by numerous other

DECISION FOR OPERATION

1. NOT DISABLED BUT PROGRESSIVE INSUFFICIENCY
   A. SUBJECTIVE—INCREASING ANGINAL ATTACKS
      INCREASING DYSPNEA
   B. OBJECTIVE—INCREASING E. C. G. CHANGES
2. DISABLED, PARTIAL OR TOTAL
   A. AFFECTING WORK
   B. DEVELOPING PSYCHONEUROTIC TENDENCY
3. NOT NECESSARILY HAD OCCLUSION IF (1.) OR (2.) ARE PRESENT
4. AGE—NO LIMIT, IF GENERAL CONDITION IS GOOD
5. SPECIAL CONSIDERATIONS
   A. HYPERTENSION IF NOT SEVERE
   B. CARDIAC ENLARGEMENT IF NOT TOO MARKED
   C. OTHER DISEASE PRESENT

FIG. 2

investigators on this subject were surveyed. The general conclusion seems to be that there are two indications for the use of radioactive iodine. It is properly used in the patient who has very severe incapacitating angina that will not respond to medical treatment, and in the patient with intractable congestive failure. These are the indications if there is no evidence of hypothyroidism. Seventy-five per cent worthwhile improvement may be expected in the anginal patients. In the congestive failure patients, 60% will show worthwhile improvement. There does not seem to be much evidence that there was any increase in longevity although the patients improved clinically. Most of these patients will need thyroid extract after treatment.

Indications for the surgical treatment of coronary heart disease are given in figure 2. (1) The patient is not disabled but he has progressive insufficiency, either subjectively or objectively with increasing anginal attacks, increasing dyspnea, or increasing ECG changes. (2) He is disabled either partially or totally, affecting his work or developing psychoneurotic tendencies.

Many surgeons feel that psychoneurosis is a contraindication to an operative procedure. Most cardiac coronary patients have a certain amount of psychoneurosis for fear of an impending attack. They know what might happen if at any time their angina cannot be controlled. If we can have a successful result with improvement in these patients then their psychoneurosis will improve.

(3) Not necessarily having had an occlusion; in other words, the patient may have severe angina which may make him more incapacitated yet he has never actually had an infarction.

(4) There is no limit to the age if the patient's condition is good.

(5) If blood pressure is not too high, if cardiac enlargement is not too great, or other diseases present not too severe, then surgical treatment can be considered. These must, of course, be individually evaluated.

The contra-indications to the procedure are given in figure 3. (1) Mild angina or angina that does not incapacitate the patient is always a medical problem and should be treated medically. I think surgery should be reserved for only those patients that can no longer be controlled; the patient having sufficient disability that he just can't quite do his work, or he is becoming more incapacitated as described in figure 2. I have not been bold enough to operate on patients with status anginosis (2) and I don't think I will in the future. Results by a good many surgeons are not very good and even though patients survive the operation, which a lot of them do not, they still continue to have considerable difficulty and pain following the operation. (3) Marked hypertension is a contraindication. (4) Too rapid progression of ECG

CONTRA-INDICATIONS TO CORONARY HEART SURGERY

1. MILD ANGINA
2. STATUS ANGINOSIS
3. MARKED HYPERTENSION
4. TOO RAPID PROGRESSIVE E. C. G. CHANGES
5. CARDIAC FAILURE
6. GENERALIZED MARKED CARDIAC ENLARGEMENT
7. RECENT INFARCTION
8. OTHER DISEASES OF A SERIOUS NATURE

FIG. 3

changes may indicate that the patient is bordering on an infarction. It is best to intensify the medical treatment of this patient until he improves and then consider him for surgical treatment at a later date.

(5) Cardiac failure, of course, is a contra-indication if it is intractable. If it is corrective then the patient may have surgical treatment at a later time. (6) Generalized marked cardiac enlargement, or a (7) recent infarction, or (8) other diseases of a more serious nature are again individually evaluated.

The actual surgical treatment of these patients is not too difficult, but, these coronary patients who have anginal pain and have myocardial insufficiency, but have never had an actual occlusion, are not too good a surgical risk. They can be carried through the operation but I think at least half of them will need help to survive. A good percentage tend to have a drop in blood pressure during the surgical procedure. Before the operation there should be a careful renal evaluation. A certain percentage of these patients will need a vasopressor agent for several days following the operation. It is mandatory to know in advance that the kidneys can carry this increased output, particularly in the first day or two, until the patient is over the effects of the anesthesia and any vasopressor substance used. It is not advisable to admit these patients to the hospital too many days before the operation. They can become quite apprehensive and an apprehensive patient, as the time draws near, may actually develop an infarction or occlusion on the morning of the operation. It is best to bring the patient in the hospital only two or three days in advance and sedate well, particularly the night before and the morning of the operation. At the actual induction of anesthesia, pentothal sodium is used initially. The patient should be well ventilated with oxygen and a few minutes allowed to elapse before the endotracheal tube is rapidly passed, at which time the patient is again well ventilated. Needless to say, the anesthetist must be constantly aware of the fact that the blood pressure may drop at any time during this induction and a close watch made of the pulse and the blood pressure. A cardioscope is always used. If the QRS interval tends to widen, the surgery is cancelled provided the incision has not been made. Another critical period is when the patient is turned to the right lateral position. If pressure drops, the anesthetist should be prepared to immediately start a vasopressor agent. Levophed or Neosynephrine are usually used, and if the pressure promptly elevates over 90 systolic the operation may be continued. If it does not, the operation should be postponed as the surgeon is inviting a mortality. Immediately the chest is opened is another favorite time for the pressure to drop, and in at least three of my first five patients the pressure did drop when the chest was opened. If the pressure drops, the anesthetist should immediately start a vasopresser agent and a strong concentration should be used. Neosynephrine is usually used first. If it takes a very rapid drip to keep the blood pressure over 90 systolic then a switch to

Levophed is made. Again, if it takes a rapid drip to keep the blood pressure elevated the concentration is increased to prevent overloading the patient with fluids. A very large amount of Levophed can be used. It does not matter how much; 20, 30, 40, or 50 mg. per liter of glucose in water can be used to cut down the amount of fluid the kidneys have to handle following the operation. Sufficient should be used to keep the blood pressure up with a slow drip. An important factor that must be considered is the possibility of a slough following or during the treatment. This can usually be avoided. One must watch the area between the needle site and the shoulder, or the needle site and the groin along the venous flow. The vein area with Levophed will always be cool and as time passes will also become red. This should not cause alarm. Whenever there is the least bit of whiteness appearing there is impending necrosis. Immediately, and by immediately I mean as soon as can be arranged, the needle should be changed to some other site. A good plan is as follows: start in one arm and if a blanching area begins to occur switch to the other leg or arm, and then switch as often as necessary to a new site. Usually within two or three days the Levophed can be diluted sufficiently so that the danger of slough has passed. No tendency to necrosis or blanching has occurred when the concentration can be kept below 3 mg. to 12 mg. per liter of fluid. An example of a high concentration of Levophed being needed was in a patient who underwent surgery other than for coronary disease, and whose blood pressure dropped following the operation. 48 mg. of Levophed in each liter of glucose was used and 6000 cc of fluid was given in the first 24 hours. The next day the amount of fluid and Levophed could be slowly reduced by half, and within four days the Levophed was stopped. The site of injection was changed three times.

I would like to present my own small series of cases. Five patients have had sufficient time elapse for surgical evaluation. Three had the Vineberg procedure and the last two had the Beck I procedure. My

Courtesy AFIP

FIG. 4. Group photo of five revascularized patients.

first Vineberg was simply an implantation of the internal mammary artery and in the last two I added on the other minor surgical procedures that I listed in figure 1. The Beck I is a considerably more simple operation than the Vineberg. The Vineberg requires a very meticulous dissection of the internal mammary artery without handling or grasping the artery. If the artery is grasped with a forceps, a clot or thrombus is invited. Using the Beck I, the operating time is reduced by half. The operation is not particularly difficult; the patient tolerates it better; the convalescence period is shorter; and, these patients usually can return to work more quickly. In these five patients there has been no mortality. Four have been completely relieved of pain and the fifth one classifies himself as 70% improved. The two patients with the Beck procedure have had no further anginal pain from the time of the surgical operation until the present time. These of course are my two latest patients. The patients that have had a previous occlusion seem to tolerate surgical interference and surgical trauma a little better than the patients that have only angina. These patients, to survive, have developed a certain amount of collateral circulation and can tolerate this manipulation of the heart; whereas, the anginal patients do not have any collateral circulation and therefore, are often the type that will need a vasopressor agent following or during the opera-

tion. A brief description of the five patients follows.

CASE I. H.L., age 36 at time of surgical treatment. Patient is an insurance salesman. In 1950 he had a posterior infarction, did well until his next attack May 8, 1953, at which time he had an anterior infarction. He continued to have substernal pain from May 1953 until time of the surgical treatment November 16, 1953. He turned down one promotion and was reaching the point of becoming quite disabled. Considerable nitroglycerin was required to maintain his work. He was taking numerous tablets daily. He was quite dyspneic on climbing stairs. In addition, he is one of the survivors of the Japanese Prison Ship that was sunk during World War II. Surgical procedure performed was a Vineberg procedure. Patient required Levophed for 36 hours, starting from the time the chest was opened, to maintain his blood pressure. Since the operation he has gradually improved and after approximately three months required no medication, and at the present time has no limitation to his activities. This man works very hard, averaging 16 to 18 hours a day. A recent electrocardiogram has shown definite improvement over his pre-operative electrocardiogram. The patient considers himself completely free of pain and dyspnea.

CASE II; J.C., age 42 at time of surgical treatment. This man had anginal pain starting December 1952. His work was operator at Carbide and Carbon Chemical Corporation. He had never had an actual occlusion but had become quite disabled with the severe anginal pain. It had reached the point where eating would cause pain, so he therefore quit eating solids and drank liquids at intervals during the day. He was unable to work. Mild to moderate exertion would cause anginal pain. Patient was extremely upset, apprehensive, and seemed to be tense most of the time. Twice he had been taken to the hospital in extreme pain, requiring oxygen. Neosynephrine at first, and then Levophed was given from opening of the chest at time of surgical treatment, May 27, 1955, and for the following six days. He returned to work after the operation and has been able to indulge in considerable strenuous exercise which he was not capable of doing before, such as deer hunting and ice skating. He has mild angina, "nothing like it was before," but he may go for days with no pain and then again he may have several mild attacks. He classifies himself as 70% improved. Operation was a Vineberg procedure.

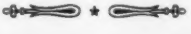
CASE III; L.W., age 42 at time of surgical treatment, June 21, 1955. This man's angina occurred one year before his first occlusion which was in November 1954. Patient was also moderately hypertensive. His work is that of a salesman and he was unable to devote his full time to his work because of severe pain and in the last few months almost complete disability. April 1955 he had a repeat attack which showed myocardial insufficiency and subendothelial infarction could not be ruled out. His pre-operative blood pressure was 170-190/90-110. Neosynephrine was required for twenty minutes during the operation but not postoperative. This man rates himself as completely recovered, requiring no medication and having no angina or dyspnea, and he works 12 to 14 hours a day. He has driven as much as 600 miles a day in his occupation as salesman. His hypertension persists.

CASE IV; F.C., age 41 at time of surgical treatment. This man had an original heart attack August 1954 and since then, four light attacks. He had been maintained on medical treatment with only fair results. Walking or slight exertion would cause constriction in his neck and substernal pain. He had not been back to work since his last attack in October 1955. There was no change, however, on electrocardiogram since July 1955. On December 8, 1955 a Beck I procedure was performed, except that talc instead of asbestos was used in the pericardial sac. Patient returned to work March 12, 1956 and has had no further anginal pain since his operation. Recent electrocardiogram showed definite improvement as compared with his pre-operative electrocardiogram.

CASE V; D.E., age 36 at time of surgical treatment. This young woman had been having severe anginal pain for over a year. She was in the hospital two months before her surgical treatment for evaluation and sent home. She came back stating that she was unable to work, her pain was more frequent, and was not being relieved sufficiently with the nitroglycerin. Whenever she took nitroglycerin or any similar drug she would develop an intense headache. February 24, 1956 a Beck I procedure, using talc in the pericardium, was performed. She required Levophed toward the end of her operation and for the following four days. She has had no anginal pain since the operation. At six weeks she could mop floors and do work she had not been able to do for the last year. She has since returned to work and has no complaints. There is no anginal pain and no dyspnea.

In summary then, I have these five patients; four of them with excellent results, and the fifth with 70% improvement. It is not a fair comparison but, in the same interval, four other patients were referred; two I actually examined, and the other two were told by their own physician that surgical treatment should be done. All four refused surgery at that time and deferred operation. All four had further occlusion and all four are dead.

In conclusion, I believe that we can help these patients. We can improve their life expectancy and we can restore many of these cripples to work. I know that this is not the final answer and someday there will be a better procedure or procedures to revascularize the heart.



REFERENCES

[1] Beck, Claude S.: The Development of a New Blood Supply to the Heart by Operation; Annals of Surgery, 102:801, 1935.

[2] Evans, J. A., and Poppen, J. L.: Resection of Anginal Pathways for Relief of Anginal Pain; New England Journal of Medicine, 249:791, 1953.

[3] Beck, Claude S.: The Development of a New Blood Supply to the Heart by Operation; Annals of Surgery, 102:801, 1935.

[4] Beck, Claude S.: and others, Revascularization of the Heart by Graft of Systemic Artery into the Coronary Sinus; J.A.M.A., 137:436, 1948.

[5] Idem.

[6] Idem.

[7] Beck, Claude S.: and others, Communications Between the Coronary Arteries Produced by the Application of Inflammatory Agents to the Surface of the Heart; Annals of Surgery, 118:34, 1943.

[8] Vineberg, A. M.: Development of Anastomosis Between Coronary Vessels and Transplanted Internal Mammary Artery; Canadian M.A.J., 55:117, 1946.

[9] Beck, Claude S., and Leighninger, D. S.: Scientific Basis for the Surgical Treatment of Coronary Artery Disease; J.A.M.A., 1264, Nov. 1955.

[10] Hellerstein, Herman, Kopel: The Surgical Treatment of Acquired Non-Rheumatic Heart Disease; Journal Medical Assn. of Georgia, 43:857, 1954.

[11] Vineberg, A., and Buller, W.: Technical Factors Which Favor Mammary Coronary Anastomosis; J.Th. Surg., 30:411, 1955.

[12] Plachta, A., Thompson, S. A., Speer, F. D.: Pericardial & Myocardial Vascularization Following Cardiopericardiopexy; A.M.A. Arch. Path., 59:151, 1955.

[13] Jaffee, and Associates: Radio-active Treatment of Euthyroid Cardiac Disease J.A.M.A., 139:434, 1955.

Vascular Lesions Associated with Heart Disease*

By

WILLIAM C. VON GLAHN, M.D.

Professor of Pathology, Louisiana State University School of Medicine, New Orleans, La.

THE vascular lesions associated with cardiac disease fall naturally into two groups. There are those that result from infected emboli and those that occur independently of the cardiac lesion.

An excellent example of the infected embolic lesions is found in subacute bacterial endocarditis in the form of mycotic aneurysms that may involve any of the arteries of large caliber as cerebral, mesenteric, renal, gluteal and coronary. The infection spreads to the wall of the artery, that undergoes necrosis, bulges and finally is destroyed only a few scattered fragments of elastic tissue remaining; the sac is filled with the embolus and secondary thrombus about it. By direct extension of the infection from the aortic leaflets, mycotic aneurysms may form in the aorta.

In acute endocarditis, the embolic lesions are less likely to form mycotic aneurysms and in those due to staphylococcus aureus, abscesses are commonly found.

In rheumatic disease there occur vascular lesions that are not the result of emboli. In the aorta is found an elevated translucent yellowish plaque with wrinkled surface, and having a tawny yellow color. Histologically, there is occasionally found swelling of fibrillar material, bordered by palisades of large mononuclear cells, and also focal collections of polymorphonuclear leucocytes amongst which are cells with distorted nuclei. More frequent are accumulations of large mononuclear cells held in rows by the elastic fibers and along the vasa vasorum are large mononuclear cells, polymorphonuclear leucocytes and sometimes eosinophiles. The adjacent elastic fibers are spread apart and some are fragmented. Dense avascular scars remain when the lesion is healed. Aschoff nodules are found in the adventitia. Aneurysms following rheumatic aortitis are very rare. Lesions in the pulmonary artery similar to those in the aorta have been described.

A distinctive arteritis also occurs in rheumatic fever. There is a fibrinous exudate beneath the endothelium, that may extend into and through the vessel wall often associated with hemorrhage. The wall at times is necrotic; polymorphonuclear neutrophiles and eosinophiles, large mononuclear cells and cells with distorted nuclei collect about the involved vessels. The internal elastica is stretched, fragmented or ruptured. The lumen is not occluded by a thrombus. The fibrin is replaced by connective tissue and the lumen is narrowed. When there is hemorhage new capillaries are formed that empty into the original lumen, the healed lesion then resembling an organized and canalized thrombus.

Another lesion is the verrucous endarteritis of Holsti. The lumen of the vessel is filled with a finely granular material that distends the vessel. About the vessel are polymorphonuclear leucocytes and eosinophiles. The granular material is covered and invaded by endothelial cells. I have seen this lesion only in the heart and kidneys. Holsti described the endarteritis in a series of cases that he designated "arthro-nephro-cardiopathies" and in the tonsils of a rheumatic patient.

Another type of arteritis associated with cardiac disease is that attributed to hypersensitivity. The lesion apparently begins in the media; there is an intense acute inflammatory reaction, and a thick layer of fibrin is deposited on the intimal surface. The vessel wall is completely destroyed in places with the formation of an aneurysm.

Lupus erythematosus is another disease in which cardiac and vascular lesions are

* Presented at the Post Graduate Seminar on Diseases of the Heart, Armed Forces Institute of Pathology, Washington, D.C., May 14-17, 1956.

found. The most specific vascular lesion is in the spleen, where the central arteries of the Malpighian bodies are surrounded by concentric layers of connective tissue cells and later by layers of collagen. Not all of these arterioles are equally involved. Other arterioles are acutely inflamed, their walls edematous and infiltrated by polymorphonuclear leucocytes. The glomeruli of the kidneys show the wire-loop lesions and arteries in other parts of the body may be acutely inflamed and their walls necrotic.

Any discussion of the vascular lesions associated with cardiac disease would be incomplete without discussing some of the vascular lesions that may involve the coronary arteries.

In syphilis, gummata of the myocardium may be present. I have seen one case in which there was a syphilitic lesion involving the endocardium of the left auricle that in every way, both grossly and histologically, was an exact replica of the changes found in syphilitic aortitis. The common way in which syphilis affects the heart is due to involvement of the aortic valves and stenosis or occlusion of the orifices of the coronary arteries. It is in those cases where the coronary arteries have an unusually high origin that they are occluded or stenosed. Rarely a coronary artery may show the changes of a mesarteritis with adventitial and medial infiltration of plasma cells and lymphocytes.

The coronary arteries may be involved in giant cell arteritis, that is best seen in the temporal arteries, where areas of patchy medial necrosis occur with fragmentation of the internal elastic membrane. In these areas multinucleated giant cells collect just beneath the elastica, and similar giant cells are also found in other parts of the media. Lymphocytes accumulate in the areas of involvement and other types of cells may be present. Thrombosis may occur though more often thrombi are absent. The intima is thickened by the proliferation of connective tissue and the lumen is markedly reduced in size.

Giant cell aortitis, similar to giant cell arteritis, is described. In the media there is necrosis, with giant cells and lymphocytes. Fragmentation and destruction of the elastica is widespread but is not so marked as in syphilis. In a recent case of giant cell aortitis, a granulomatous lesion, consisting of giant cells and large mononuclear cells, was present in one of the coronary arteries.

Thromboangiitis obliterans has been reported in the coronary arteries. In the peripheral arteries, the initial change is the formation of granulomata in the intima; these are collections of large mononuclear cells and giant cells. The lumen is filled with polymorphonuclear neutrophiles and eosinophiles and similar cells are found in the media. Thrombi form in the lumen, apparently on either side of the foci where the granulomata are formed. The thrombi are organized and canalized. Granulomata similar to those in the intima of the arteries are present in the veins and later organized and canalized thrombi obliterate the lumina.

Periarteritis or polyarteritis nodosa involves the peripheral and coronary arteries. The first change is a necrosis of a portion of the media with an acute inflammatory reaction. Eosinophiles are often present with fibrin in and about the area of necrosis. The elastic lamellae are destroyed. Giant cells are sometimes found. The process may spread circumferentially to involve the entire wall of the artery. Thrombosis and aneurysm formation are frequent.

These various lesions, that have been mentioned, are easily separated into two groups, the granulomatous and the acute inflammatory. In the granulomatous group are syphilis, giant cell arteritis and aortitis, thromboangiitis obliterans and the rheumatic lesions. Hypersensitivity arteritis, polyarteritis nodosa, lupus erythematosus and mycotic aneurysms are lesions of an acute inflammatory nature. That a lesion of an artery belonging in one or the other of these two groups may have an almost identical histological appearance or closely resemble another lesion in the same or the other group cannot be taken as an indication that there is a common etiology. Undoubtedly many different agents can damage an artery and there be no histologic difference in the changes produced in the artery.

EDITORIAL

Aging

IN THE past fifty years life expectancy at birth in the United States has been advanced to 70 years, thereby fulfilling the statement in Proverbs "the days of our years are three score and ten."

From the very conception of human life the mortality of the human embryo has a better chance of maturing, and from the birth of the child more years are promised him now than at the turn of the century. All this has been brought about by increased knowledge. But knowledge without application would never have broadened the span of life in the United States. It is the application of that knowledge that has obstructed the path of the Grim Reaper.

By increasing the span of human life in the United States have we increased the problems? Very definitely we have. Even though the everyday problems were the same as years ago we would add to them by the days we have added to man's life in America.

One of the problems facing us, and by no means a small problem, is that of the older person. What do we mean by the "older person"? When is a person old? When has he arrived at a useless age? We do not infer that an old person is useless. But just when is a person old; at 50, 60, 70, or even 80 years? Probably for business reasons we must set an arbitrary age, anywhere from 50-65 years. But is that person separated from a business (or from the military service) during those years necessarily a robot from then on? Surely he can be useful. Whether he wants to be or not is another matter.

Conditioning for the later years in life should be a concern of the individual during his active years. Once he has conditioned himself society must provide the opportunities for a useful (not to be confused with a compensable) place. Otherwise the individual finds himself on a turbulent sea tossed to and fro by the waves of uncertainty and despair.

This big problem of aging is one which the Department of Health, Education, and Welfare is studying. The Department's bulletin, *Aging,* is full of information and for those interested in the problem it is worth while reading.

"The management of the chronic and degenerative diseases, which so often strike man at the height of his productivity and financial responsibility, presents one of the most difficult problems faced by the physicians of today." AIMS C. MCGUINNESS, M.D., Special Assistant (for Health and Medical Affairs) to the Secretary, Dep't. of Health, Education, and Welfare.

Around the World

(Ser. II, No. 8)

By
CLAUDIUS F. MAYER, M.D.

HAWAII, the largest and southeasternmost of the Hawaiian Islands, can be reached by short trip from Honolulu. Half of the island is *Mauna Loa,* a large volcanic mountain, considered one of the largest single land masses of the world. The side of this mountain is a less than 7% slope, and its summit, at 13,680 ft above sea-level, is at a distance of some 40 miles. A trip from Hilo, the island's principal city near sea-level, to the summit leads through a variety of climatic and corresponding vegetation zones. On the slope, at 11,134 ft above sea-level, the U. S. WEATHER Bureau has erected a new observatory unit where all kinds of *meteorological and bioclimatic studies* can be arranged in the future. A group of National Geographic scientists has recently completed there a series of spectrographic observations of the atmosphere of Mars. Special studies of solar radiation are scheduled for the coming spring at the observatory. This research center can be also "borrowed" for carrying out any suitable biomedical project.

The practice of *occupational medicine in Australia* has received little recognition. According to an investigating committee, which just finished its survey, only in New South Wales and Queensland is there any real attempt to provide some degree of instruction in occupational medicine for medical students. New South Wales also has some kind of postgraduate instruction in industrial hygiene, but there is no clinical teaching, nor are there hospital facilities available for the staff. Australian industries are mostly closed on Saturdays, and medical students have no chance to visit them. Photographs and movies of industries cannot substitute for real life problems. In Victoria and South Australia, teaching facilities for industrial medicine are negligible. Medical services provided to the employees of most major industries are quite inadequate. In New South Wales the number of full-time industrial medical officers is exactly 3, in Victoria 3, in Queensland 1, and in South Australia 1. A number of large factories, with 1,500 to 2,000 employees, make no provision for regular medical attendance.

Attempts are made by the Administration of the *Pacific-New Guinea Region* to encourage the *preservation of native arts,* crafts, and customs. One such custom is the wearing of the *upi* hat. The hat is attached only to long strands of the wearer's hair. The *upi* is worn for several years and never removed. An official reports that he used some lysol under the headgear of *upis* working for him to counteract the *mus-mus* until one day an old chief came along and explained that the official was interfering with a part of the custom of initiation. The livestock underneath the *upi* was part and parcel of the tribal rite. One of the anthropologists globetrotting around this area asserted that the New Guinea pigmies are *happy because they eat beetles* that contain an abundance of the happiness-inducing vitamin-T.

Hong Kong has a harbor more beautiful than Rio de Janeiro, and an atmosphere as cosmopolitan as Paris. With several other islands, the total area of the British Crown Colony is ca 390 sq. miles, with a population of nearly 3 million. For its mixed-up terrain and messed-up culture it is a fascinating place for tourists. The *Hong Kong* government approved the *plans for a mammoth hospital* of 1,273 beds to be completed for about 9 million dollars. The New Kowloon General Hospital will be 13 floors, and it will have all modern facilities of therapy.

Earlier observers stated that *heart infarction* and angina pectoris were rarely seen

in China although hypertensive heart disease was common. Similar statements were made concerning the people of Malaysia. A doctor of the Penang General Hospital suggests that coronary thrombosis is *less common in Southeast Asia* than in western European countries. The impression is gained that a high rate (27%) of the infarctions were the painless variety. Perhaps, for these poor people whose life is an endless chain of many pains and hardships, a pain in the chest may be alarming but of little further significance to worry about. Perhaps, the pain in the poorer man is less severe. A western observer who recently returned from a medical congress in Moskva heard that, in the past 20 years, even the Chinese had a six-times increased frequency of myocardial infarction. (By the way! *Sweden* is working on a suprasonic *radar-type of apparatus* which is supposed to show the exact site and size of a heart infarction.)

Psychosomatic diseases in India reflect the social pattern of the country. In rural areas where people are living with hardly an inhibition there is almost a state of mental and emotional equilibrium, and almost complete freedom of psychosomatic troubles. People living in urban areas have not much trouble either until they are "westernized." Those women in the cities who are in constant struggle and competition with their mothers-in-law may suffer from chronic diarrhea ("riddance phenomenon"), fever and conversion hysteria. Since sex is a taboo among the Hindus, surreptitious sexual activities among city dwellers may produce a feeling of guilt, and its psychoneurotic sequelae. Psychoanalysts in India have difficulty in interviewing female patients who will frequently reveal their personal background under sodium amytal only. The lower status of the female in India makes all female children envious of the male, and is a basic source of sibling rivalry. It is possible that villagers, in addition to their placid attitude toward life, have a great outlet of their pent-up emotions in their agricultural field work with the spade and plough.

The *Valley of the Spiti River* is the most inaccessible part of India. It is a wedge on the Tibetan border, between Kashmir and the State of Bashadr on the Sutley. At some places, the mile-wide Spiti River forms the boundary line between India and Tibet, surrounded by a very dramatic landscape. The valley is inhabited by *some 5,000 Tibetans* who are occupying about 50 villages. Not so long ago, it was visited by an expedition from Cambridge which had the opportunity to watch the attempt of the Indian government at the modernization of this remote spot of culture. The local government is in the hands of the largest landholder who is called *nonno*. The majority of the villagers are landless. Of course, there are Buddhist monasteries, five of them, with celibate monks who are fed and supported by their families. The birthrate is rather low in Spiti since many a young man, being absorbed by the monasteries, is removed from the marriage market. (The total population was 3,700 in 1900; now it is exactly 4,800.)

Formerly, the monks used to travel to Lhasa once a year, but, since Tibet passed under the control of communist China, this monastic duty became very difficult (passports, visa, etc.). The strength of these people is remarkable as witnessed by the loads which they are able to carry up the steep mountain slopes. For this reason, one may think that they are healthy. Indeed, there are many among them weather-beaten, toothless, and wrinkled; yet, the entire population is infected with *venereal disease, the scourge of hill people.* Many show the stigma of congenital syphilis: bridgeless noses, desiccated and yellow gums, widely set teeth. There are, of course, no statistical figures about the rate of infantile mortality and psychosis.

They established a marvellous primitive irrigation system, and have no fear of famine though they have practically no rainfall. Since the people seem happy with their present state it may be feared that further attempt at civilization may result in a complete disruption of their life and a cultural disas-

ter. Recently, the *Punjab government sent up a doctor* (Dr. Massey) to Spiti who keeps on travelling up and down the valley, with a caravan of 2 orderlies and 14 mules, dispensing DDT, sulfa drugs and vaseline. But the DDT was scorned, the sulfa-drugs, intended to be a cure for gonorrhea, are looked upon as candy, and the doctor is mobbed everywhere by the small children for the pretty white pills. The vaseline is greatly appreciated by all people and used as a protective smear against the icy winter blizzards.

During a two-year period (1953-55) there have been 3,910 dermatological patients treated at Rockcliffe, in the *Royal Canadian Air Force Hospital.* During this time, only 12 cases of syphilis were detected (3 prenatal, 8 latent or late, and 1 primary). The *low incidence of syphilis* at this Canadian Hospital is in line with the reports from clinics and hospitals in North America and Europe where venereologists have difficulty in obtaining clinical material for teaching.

Thus, also in the *Romanian Army,* where the *rate of syphilitic infection* was 23.5 per thousand in 1936, the frequency of the diseases has dropped to 0.33 per thousand in 1955. Of all the cases detected in the Romanian Army, 14.9% were primary, and 85.1% were latent cases of syphilis. Since 1948, syphilitics, in Romania are required to stay in the hospital during the entire period of treatment of the acute attack. There, the treatment is still a combination of arsenicals and bismuth with penicillin.

In memoriam of Roger Buddle, late surgeon-commander in the Royal Navy and a naturalist, a retired surgeon-captain of H.M.N. recalls the event of *an unusual post-mortem* which he and the naturalist had performed when some years ago they were stationed *at the Singapore Naval Base.* On the upper reaches of the tidal estuary of the "Bukit Sembawang," near the Asiatic Hospital of the Base, the natives shot a 7-8 ft crocodile and brought the body to the hospital for examination. This reptile had been held responsible for the disappearance of more than one Chinese within a few years. In presence of a large crowd of interested spectators—most of them in anticipation of a feast—the animal's stomach was opened. Surely, its contents proved that the crocodile had made a meal of a Chinese. Not only the radius and ulna and some carpal bones were found but also a Chinese tunic complete with buttons, with dicemen and a dicebox in the pockets, and also the red canvas sail of a Chinese sampan which the post mortem examiners pulled out yard by yard, almost performing a conjuror's trick. They also hauled out 3 large stones, ca. 14 lb in weight, which, in the belief of a Malay bystander, the crocodile had retained as a memento of the happy days it spent in some three rivers.

One of our *Finnish* colleagues made a statistical study of the *family of physicians* of his country. He interviewed 2,170 doctors of whom 1,709 were men. Most of the men (90%) and the majority of the women (60%) were married, assuming the ties of matrimony about the 27th or 28th year of life. The wives of 60% of the Finnish physicians are themselves doctors or nurses. Only 10% of the doctors married twice, and only a very few (0.5%) risked it the third time. . . . *Multa paucis!*

SUSTAINING MEMBERS

It is a privilege to list the firms who have joined The Association of Military Surgeons as Sustaining Members. We gratefully acknowledge their support.

ABBOTT LABORATORIES
ASTRA PHARMACEUTICAL PRODUCTS, INC.
AYERST LABORATORIES
BAXTER LABORATORIES, INC.
BECTON, DICKINSON AND COMPANY
BURROUGHS WELLCOME & CO. (U.S.A.) INC.
CIBA PHARMACEUTICAL PRODUCTS, INC.
COOK-WAITE LABORATORIES, INC.
CUTTER LABORATORIES
EATON LABORATORIES, DIVISION OF THE NORWICH PHARMACAL CO.
GENERAL ELECTRIC COMPANY
HOFFMANN-LA ROCHE, INC.
JOHNSON & JOHNSON
LEDERLE LABORATORIES DIVISION, AMERICAN CYANAMID CO.
LILLY, ELI, AND COMPANY
MALLINCKRODT CHEMICAL WORKS
MEAD JOHNSON & COMPANY
MERCK & CO., INC.
ORTHOPEDIC EQUIPMENT COMPANY
PARKE, DAVIS & COMPANY
PFIZER, CHAS. & CO., INC.
PICKER X-RAY CORPORATION
PROFEXRAY, INCORPORATED
RITTER COMPANY, INC.
SCHERING CORPORATION
SEARLE, G. D., & CO.
SQUIBB, E. R., & SONS, DIVISION OF OLIN MATHIESON CHEMICAL CORP.
STEPHENSON CORPORATION
STERILON CORPORATION
WARNER-CHILCOTT LABORATORIES
WINTHROP LABORATORIES, INC.
WYETH LABORATORIES

ASSOCIATION NOTES

Timely items of general interest are accepted for these columns. Deadline is 3rd of month preceding month of issue.

Department of Defense

Ass't Secretary (Health & Medical)—HON. FRANK B. BERRY, M.D.

Deputy Ass't Sec'y—HON. EDW. H. CUSHING, M.D.

ARMED FORCES DAY

The tenth anniversary of military unification and the fiftieth anniversary of military aviation will be keynoted in the 1957 observance of Armed Forces Day, May 18. The slogan again is "Power for Peace."

Military aviation was established on August 1, 1907 in the Aeronautical Division of the Office, Chief Signal Officer, U. S. Army. Naval aviation dates from its first aircraft order May 8, 1911. The U. S. Air Force was established as an independent Department in 1947.

ARMED FORCES STRENGTH

Numerical strength of the Armed Forces on December 31, 1956 was 2,780,177. This is a decrease of 17,577 from November 30. The strength by services on December 31 was: Army, 992,290; Navy, 672,632; Marine Corps, 200,255; Air Force, 915,000.

DEPUTY DIRECTOR AFIP

Col. Joe M. Blumberg, MC, U. S. Army has been appointed Army Deputy Director of the Armed Forces Institute of Pathology. He succeeded Col. Francis E. Council, MC, who retired on March 31.

Col. Blumberg is a native of Georgia. He received his medical degree from Emory University School of Medicine in 1933, interned at the Maryland General Hospital, Baltimore, and was resident at the Baltimore City Hospital from 1934 to 1936. He practiced medicine and pathology in Baltimore from 1936 to 1941 during which time he instructed in clinical pathology and was assistant in medicine at the University of Maryland, and was assistant in clinical pathology at the University Hospital in Baltimore. He was called to active duty in the military service in 1941.

During his Army service Col. Blumberg has been on laboratory and pathology assignments. His latest duty prior to coming to the Armed Forces Institute of Pathology was as commanding officer and chief of pathology of the 406th Medical General Laboratory in Japan. He was also consultant in pathology and laboratory medicine to the Chief Surgeon, Army Forces Far East.

Army

Surgeon General—MAJ. GEN. SILAS B. HAYS

Deputy Surg. Gen.—MAJ. GEN. JAMES P. COONEY

SGO ASSIGNMENTS

Brig. General Sam Seeley, MC, who has been commanding the Valley Forge Army Hospital, Phoenixville, Pa., since his return from Europe last year, has been appointed Chief, Professional Division, Office of the Surgeon General.

Col. Paul Hayes, MC, has been named medical consultant to the Chief of the Professional Division, Surgeon General's Office. For the past two years Col. Hayes commanded the Landstuhl Army Medical Center, Landstuhl, Germany.

Lt. Col. Carrie E. Barrett, ANC, has been assigned as Chief, Army Nurse Corps Assignment Section, Personnel Division, Surgeon General's Office. She replaced Lt. Col. Mabel G. Stott who has been assigned as Chief, Nursing Service, U. S. Army Hospital, Fort Belvoir, Va.

Maj. Mary Catherine Jordan, ANC, has been appointed as Assistant Chief of the Nurse Assignment Section, Surgeon General's Office.

NEW ASSIGNMENTS

Brig. General Louis H. Ginn, MC, has been transferred from Fort Sam Houston, Texas, to William Beaumont Army Hospital at El Paso, Texas, where he will be in command of that hospital. He succeeds Colonel Abner Zehm, MC, who has been transferred to Fort Ord, Calif.

RETIRED

Major General James O. Gillespie, MC, Chief of the Professional Services Division, Office of the Surgeon General, retired March 31. He will make his home on the west coast.

MILITARY MEDICINE COURSE

The fifth class of Military Medicine and Allied Sciences presented annually by the Walter Reed Army Institute of Research to develop highly qualified professional leadership at Army medical research, teaching and treatment centers, will start September 3.

Fifteen medical officers who have completed formal residency training in a specialty will be selected for the nine-month course, said to have no counterpart in the United States. No attempt will be made to cover clinical subjects in a textbook fashion or to review generally available textbook data. Basic mechanisms are to be studied, recent advances in the sciences examined and correlation made between the various areas of science.

A highlight of the class commencements is the awarding of the Hoff Medal, established to commemorate Col. A. H. Hoff and given to the students attaining the highest class proficiency. The medal was founded by Col. John Van Rensselaer Hoff in 1897 and first awarded in 1902.

EDUCATION CONFERENCE

Army educators responsible for in-service medical training held their seventh annual conference at the Walter Reed Army Medical Center in February. This was a two-day conference with Col. Byron L. Steger, MC, Chief, Education and Training Division, Office of the Surgeon General, as conference moderator. Civilian educational consultants present were: Dr. Fiorindo A. Simeone, Western Reserve University School of Medicine; and Dr. Neil L. Crone, Harvard University School of Business Administration.

The purpose of the conference was to discuss changes recommended at the 1956 conference and propose measures to be taken for the next twelve months.

BURMESE WACS VISIT WRAMC

U. S. Army Photo

(L to R) Lt. Daw Hla Kyin, Lt. Daw Khin Hta, Lt. Daw Mya Thein.

Recently six members of the Burmese Women's Army Corps visited Walter Reed Army Medical Center, Washington, D.C. In the above picture three of the officers are shown examining equipment in the Electrocardiograph Clinic.

KOREAN OFFICER AT AMSS

A Korean medical officer, Cho Yung Sun, attending the course in hospital administration at the Army Medical Field Service

School, Fort Sam Houston, Texas, recently had the insignia of his new rank pinned on him by the Commandant, Brig. General Elbert DeCoursey, and the Assistant Director of the Department of Administration, Col. Sam A. Edwards.

Before coming to the United States as a student, Colonel Cho was chief of Administration and Personnel in the Office of the Korean Surgeon General.

U. S. Army Photo

(L to R) Brig. Gen. Elbert DeCoursey, Col. Cho Yung Sun, Col. Sam A. Edwards.

METABOLISM IN TRAUMA

Some of the top medical men of the country, members of the sub committee on metabolism in trauma (tissue changes following injury) of the National Research Council, met at Brooke Army Medical Center recently to view the research projects of the Surgical Research Unit and to discuss possible avenues of approach to further research by both civilian and military medical and scientific men.

Dr. Francis D. Moore, Professor of Surgery at Harvard University Medical School, chairman of the sub-committee, was joined by committee members Dr. Robert D. Dripps, Professor of Anesthesiology, University of Pennsylvania School of Medicine, Dr. Jerome W. Conn, Director of the Medical Research Unit of the University of Michigan. Dr. Joseph Holmes, Professor and Chief of the Laboratory and Dr. Henry Swan, Professor of Surgery at the Medical Center of the University of Colorado in the two day review and planning meeting.

Sitting in on the discussions were Colonel Robert L. Hullinghorst, Chief of Research and Development in the Office of the Army Surgeon General and one of his staff members, Major Charles Pixley, as well as three former staff members of the Surgical Research Unit whose work while in military medicine was in this field of interest. They were Dr. Curtis P. Artz, former commander of the Brooke unit and now Associate Professor of Surgery at the University of Mississippi, Dr. Eric Reiss, resident in surgery at Barnes Hospital, St. Louis, and Dr. Henry Soroff, chief resident in surgery at Western Reserve University Hospital, Cleveland. Dr. Robert Shank of the Washington University School of Medicine, St. Louis, was another participant.

CERTIFIED TO FOUNDERS GROUP

Three Army Medical Corps officers were admitted to the Founders Group in the newly recognized medical specialty of occupational medicine recently. Those so honored were: Col. John R. Hall, Jr., Chief of the Occupational Health Branch of the Preventive Medicine Division of the Surgeon General's Office; Lt. Col. Edward J. Dehne, Commanding Officer, Army Environmental Health Laboratory, Edgewood, Md., and Maj. Gilbert H. Collings, specialist in occupational medicine at the Laboratory.

DR. HILLEMAN HONORED

The Ninth Annual Arthur S. Flemming Award was presented to Dr. Maurice R. Hilleman, Chief of the Respiratory Disease Department, Walter Reed Army Institute of Research, by the Junior Chamber of Commerce, Washington, D.C. on February 14. The award was given in recognition of his discovery of the "RI Virus," a family of viruses which cause respiratory diseases other than the common cold.

HONORED

Col. William L. Thompson, MC, U. S. Army, Retired, was honored recently at a meeting of the combined session of the

American College of Radiology and the Association of Teachers of Radiology in Chicago.

The Special Award of Honor was given for his outstanding achievement, tireless devotion, dedicated leadership, and exemplary effort as Chief of the Registry of Radiologic Pathology at the Armed Forces Institute of Pathology which position he has held since June 1950.

ASSIGNED FIRST ARMY HQ.

Major Charles A. Coe, Jr., has been assigned as Chief, Medical Plans and Training Branch, First U. S. Army Medical Section, Governors Island, New York.

During World War II he served for three years on Saipan, Mariannas. During the Korean Conflict he was Battalion Medical Assistant and Battalion Operations and Training Officer of the Third Infantry Division Medical Battalion.

Major Coe has just returned from a special assignment in Thailand.

PHYSICAL THERAPIST TO FAR EAST

Major Isabelle M. Desmond, AMSC, will leave in August for Japan to be physical therapy consultant to the Surgeon of the United States Forces in the Far East. She will be stationed at the Tokyo Army Hospital as Chief of the Physical Therapy Section. She replaces Major Genevieve S. Beard, AMSC.

TO SAUDI ARABIA

In order to further the treatment of young Prince Mashhur of Saudi Arabia and to assist in the training of attendants who are to carry on the treatment of the Prince, two officers of the Army Medical Service and one civilian were sent to that country.

Those sent from Walter Reed Army Medical Center were Lt. Colonel Aniello Mastellone, MC, Chief of the Physical Therapy Section, Lieutenant Howard A. Appleby, Jr., also of the Physical Therapy Section, and Mr. Andrew Matzell, Orthopedic Technician. The temporary duty was to be for thirty days.

HISTORIC TRADITIONS TO BE PRESERVED

In the regiments of the new "Pentomic Army" it is planned to preserve the historic traditions of the regiments. The regiments will be institutional rather than tactical. Each "parent regiment" will field a variable number of combat units, depending upon the size of the Army at any one time. Under the regimental system, the battalions of old Artillery regiments may well fire guided missiles, and the squadrons of old Cavalry regiments will reconnoiter in airplanes rather than on horseback.

Changeover to the system will be gradual, geared to conversion of the Army to the pentomic concept. Ultimately every combat unit will bear the flag of one of the Army's historic regiments.

UNIFORM WARRANTY

Be sure to get a warranty when you buy those Army uniforms. Such is the advice given by the Army. This will insure your getting the regulation uniform and material.

Navy

Surgeon General—REAR ADM. BARTHOLOMEW W. HOGAN

Deputy Surgeon General—REAR ADMIRAL BRUCE E. BRADLEY

DENTAL CORPS

The Regular Navy Dental Corps reached a peak of 864 career dental officers on February 18. This is an increase of 165 career dental officers since August 1954.

NAVY NURSE BREAKFAST

All Navy Nurses, active and inactive, and former Navy Nurses are cordially invited to attend a breakfast get-together to be held during the convention of the National League for Nursing, in Chicago.

The breakfast will be held at the Conrad Hilton Hotel, at 8:00 A.M., on Wednesday, May 8. Tickets may be purchased at the ticket booth of the convention or at the Navy Nurse Corps exhibit.

Air Force

Surgeon General—MAJ. GEN. DAN C. OGLE
Deputy Surg. Gen.—MAJ. GEN. W. H. POWELL, JR.

DELIVERS GRADUATION ADDRESS

Brig. General Harold H. Twitchell, USAF (MC), Surgeon, Continental Air Command, Mitchel Air Force Base, New York, recently delivered the graduation address to the Advanced Refresher Course for Reserve Dental Officers offered at the USAF School of Aviation Medicine, Gunter Branch, Gunter Air Force Base, Alabama.

This is the first "advanced" course to be offered by the USAF Medical Service, and to be completed by participating Dental Reservists. These twenty-five officers had previously attended the Basic Refresher Course for Reserve Dental Officers, also offered at Gunter Air Force Base.

ROCKET PLANES

Any pilot with proper training can learn to fly tomorrow's space-roving high-performance aircraft, Lt. Col. Burt Rowen told flight surgeons meeting at the Air Force School of Aviation Medicine today.

Colonel Rowen is in charge of the Human Factors Branch at the Air Force Flight Test Center, Edwards AFB, Calif., where advanced types of combat planes are evaluated before they go into regular service. A flight surgeon himself, he also is a rated pilot and a paratrooper.

To become proficient in flying rockets, a pilot must have specialized training by the Experimental Flight Test School, also at Edwards. Rockets respond differently from jets in many flight situations. And the Air Force at present lacks rocket planes with which to top off this training.

The first U. S. aircraft powered by rockets was the Bell X-1, in which Lt. Col. Charles E. Yeager broke through the sound barrier a decade ago. Its successor, the Bell X-2, set a new speed record of about 2,000 miles per hour—three times the velocity of sound—and attained an altitude unofficially reported at close to 24 miles above the earth, both in the past six months.

The X-2 crashed in the California desert a week or two after it reached the new altitude mark. North American Aviation is now building an even more advanced rocket craft, with which the Air Force hopes eventually to attain greater speeds and higher altitudes.

In the next five years, Colonel Rowen predicted, jets will be operating routinely as high as 16 miles, at speeds around March 3. Beyond that border lies the province of space flight, in rockets that need no air, either for lift or to burn their fuels.

Control of such manned missiles is largely automatic. Flight patterns are pre-set, and instruments compensate for changing conditions to a great extent.

But no machine, Colonel Rowen reminded the surgeons, can replace the pilot's own lightning judgment in emergencies, his analysis of flight characteristics, his ability to make decisions.

Public Health Service

Surgeon General—LEROY E. BURNEY, M.D.
Deputy Surg. Gen.—W. PALMER DEARING, M.D.

NATIONAL LIBRARY OF MEDICINE

President Eisenhower recently announced the appointment of ten members of the Board of Regents of the National Library of Medicine:

Ex officio members—Dr. Leroy E. Burney, Surgeon General, Public Health Service; Major Gen. S. B. Hays, Surgeon General, U. S. Army; Rear Admiral B. W. Hogan, Surgeon General, U. S. Navy; Major Gen. D. C. Ogle, Surgeon General, U. S. Air Force; Dr. William S. Middleton, Chief Medical Director, Veterans Administration; Dr. John T. Wilson, Ass't. Director for Biological and Medical Sciences, National Science Foundation; Dr. L. Quincy Mumford, Librarian of Congress.

Appointed Members—(One-year term)

Dr. Worth B. Daniels, Clinical Professor of Medicine, Georgetown University; Dr. Benjamin Spector, Professor of Anatomy, Tufts University. (Two-year term) Miss Mary Louise Marshall, Professor of Medical Bibliography, Tulane University; Dr. I. S. Ravdin, Professor of Surgery, University of Pennsylvania. (Three-year term) Dr. Basil G. Bibby, Professor of Dentistry, University of Rochester; Dr. Jean A. Curran, Bingham Associates Fund, Boston; Dr. Champ Lyons, Professor of Surgery, University of Alabama. (Four-year term) Dr. Michael E. DeBakey, Professor of Surgery, Baylor University; Dr. Thomas Francis, Jr., Professor of Epidemiology, University of Michigan; Dr. Ernest H. Volwiler, President, Abbott Laboratories.

INTERN PROGRAM NLM

The National Library of Medicine has established an intern program for library school graduates. Complete information may be obtained from the Director, National Library of Medicine, 7th St., and Independence Ave., S.W., Washington 25, D.C.

HEART DISEASE BOOKLET FOR NURSES

The Circulatory System, An Illustrated Guide for Nursing Education is a 64-page booklet designed for nursing education in heart disease. This booklet (PHS Publ. No. 482) is available for 45¢ a copy from the Superintendent of Documents, Government Printing Office, Washington 25, D.C.

AGING

Does the central nervous system show the aging process in a corresponding manner to the other systems of the body?

In a recent meeting of 30 noted researchers in the field of neurological and sensory disorders held at the National Institutes of Health, Bethesda, Maryland, some of the conferees noted that recent animal studies show that there is no significant loss of nerve cells due to aging. They suggested that this may indicate that the central nervous system is capable of life well in excess of the present life span.

In the discussion of the relationship between aging in the nervous system and the cerebral vascular system, some conferees felt that changes in the blood circulation system of the brain (such as arteriosclerosis) did not unduly influence the aging process in the nervous system. There was general agreement that vascular changes were not the only factors bearing on aging in the nervous system.

Among other points made by the conferees were the following: 1. There is a vital need for devising and utilizing new research techniques if the fine inter-relationships of the nervous system are to be understood. The electron microscope and better nerve cell staining techniques are among relatively recent developments which will help create such understanding.

2. Insight into the aging process depends more on detailed knowledge of the physiology of the nervous system than of its morphology.

3. The probing of the relationships between cells and the synapse will probably reveal more about the aging process than will study of the cells themselves.

AIR POLLUTION

More and more attention is being given to the problems involved in air pollution. There is a need for trained personnel in this field. Consequently the Public Health Service has recently announced grants totaling $90,864 to some universities and individuals for the purpose of training in the field of air pollution control.

The program covers training in both medical and engineering aspects of air pollution and provides funds to (a) state and local government agencies for training their personnel in this field of environmental health; (b) educational and training institutions for assistance in the development and support of new curricula; and (c) qualified individuals desirous of obtaining specialized training and instructions in air pollution.

Veterans Administration

Chief Medical Director—WILLIAM S. MIDDLETON, M.D.
Deputy Chief Med. Dir.—R. A. WOLFORD, M.D.

ASSIGNMENTS

Dr. Frederick J. Balsam, who has been program development chief in the physical medicine and rehabilitation service of the Veterans Administration in Washington, D.C., was transferred to the VA hospital at Ann Arbor, Mich. He will direct the physical medicine and rehabilitation service at that hospital and will hold a faculty appointment at the University of Michigan Medical School.

Tom L. Fowler has been appointed manager of the VA hospital at Alexandria, La., to fill the vacancy created by the retirement of Dr. Pattison A. Waters.

Dr. M. H. Gordon was appointed as assistant director of the central research laboratory for the nationwide evaluation of tranquilizing drugs in the Veterans Administration hospitals.

Dr. George W. Hobson was appointed as manager of the VA hospital at Excelsior Springs, Mo., to fill the vacancy created by the retirement of Dr. Paul C. Bruce.

Dr. Edward H. Mandell has been appointed manager of the VA consolidated hospital at Indianapolis to fill the vacancy created by the retirement of Dr. Earl H. Hare.

Dr. Russell E. Pleune has been appointed as manager of the VA hospital at Saginaw, Mich.

Dr. Oren T. Skouge has been appointed as manager of the VA hospital at Oklahoma City to fill the vacancy created by the retirement of Dr. Clarence E. Bates. Dr. Skouge served in the Army Medical Service from 1942 to 1946, attaining the rank of major.

Dr. Lester L. Weissmiller has been appointed as manager of the VA hospital at Rutland Heights, Mass. During World War II he served with the 135th Medical Regiment of the Army, and later as executive officer of Deshon Army General Hospital.

HEART MONITOR

A new instrument, the "Cardiac Monitor," has been developed at the Veterans Administration Hospital, Hines, Ill., for use in surgery or in non-surgical emergencies.

Standard electrocardiograph electrodes are strapped on the forearms of the patient. These pick up the cardiac impulse and feed it into the machine. The impulse is amplified by the transistor circuit and indicated on a meter.

Miscellaneous

THE JAMES STEVENS SIMMONS MEMORIAL PROFESSORSHIP FUND

Friends of the late Brigadier General James S. Simmons, U. S. Army, Retired, have given $150,000 toward an endowed professorship in his name at the Harvard School of Public Health. The Committee of Sponsors is composed of 15 prominent persons, with George Cheever Shattuck as Chairman. When accumulated income on the endowment and additional gifts have brought the Fund to $400,000, a James Stevens Simmons Professor will be appointed.

Contributions to this Fund may be sent directly to the Harvard School of Public Health, 55 Shattuck Street, Boston 15, Mass. Checks should be made payable to Harvard University. The names of all contributors will be published in University reports and recorded in the Archives.

General Simmons was well known for his work in the field of preventive medicine. He was Chief of the Preventive Medicine Service, Office of the Surgeon General of the Army from 1940 until his retirement in 1946. At that time he became Dean of the Harvard School of Public Health in Boston which position he was holding at the time of his death on July 31, 1954.

SURVEY OF BLOOD TRANSFUSION SERVICES

The Joint Blood Council has received a grant of $50,000 from the Public Health

Service to make a 2-year study of the nation's blood transfusion services.

In addition to the survey, objectives are the preparation of guidelines and standards for accreditation of blood banks, development of a glossary of terms and solution of numerous nomenclature problems, inventory of research in blood and blood derivatives, and the assembling and analysis of needed data pertaining to these objectives.

Dr. Frank E. Wilson, executive vice-president of the Joint Blood Council, will serve as study director, with Mr. Paul T. Rees as associate director.

The Joint Blood Council is a voluntary organization incorporated by five nonprofit agencies, the American Medical Association, American Association of Blood Banks, American Hospital Association, American National Red Cross, and American Society of Clinical Pathologists. The headquarters is at 1832 M St., N.W., Washington 6, D.C.

NEW DISEASE OF NERVOUS SYSTEM

"Maple sugar urine disease" has been reported by Dr. L. Emmett Holt, Jr., professor and chairman of the department of pediatrics, New York University-Bellevue Medical Center.

The first case was described in Boston about a year ago by Dr. John Menkes, now a member of the pediatric staff of Bellevue Hospital. The disease develops in young infants who appear normal at birth but who deteriorate mentally in the course of a few weeks or months and terminate fatally. A most characteristic feature of the disease is a strong odor resembling that of maple sugar found in the urine, but the abnormal substance is not maple sugar. The possibility of controlling the disease by adjusting the amino acid composition of the diet is indicated.

POST GRADUATE SYMPOSIUM

A Post Graduate Symposium on the Basic Sciences Related to Anesthesiology will be held by the University of Pittsburgh School of Medicine, June 10-14. Registration and full particulars may be obtained from the Chairman of the Committee on Graduate Medical Education, University of Pittsburgh School of Medicine, 3941 O'Hara St., Pittsburgh 13, Pa.

PG COURSE

The management of chronic kidney disease and of hypertension will be given in two post-graduate courses at the New York University Post-Graduate Medical School from June 24 through 27. Further information may be obtained from the Office of the Associate Dean, 550 First Avenue, New York 16, N.Y.

MEETINGS

The Twelfth National Industrial Health Conference will be held at Kiel Auditorium, St. Louis, Mo., April 20-26. This conference annually brings together the five organizations whose members are responsible for maintaining the health of the nation's industrial workers: the Industrial Medical Association; the American Industrial Hygiene Association; the American Association of Industrial Nurses; the American Conference of Governmental Industrial Hygienists; and the American Association of Industrial Dentists.

The American Goiter Association will hold its annual meeting at the Hotel Statler, New York, May 28-30, 1957. There will be papers and discussions dealing with the physiology and diseases of the thyroid gland. Further information may be obtained from John C. McClintock, M.D., 149½ Washington Ave., Albany 10, N.Y.

The American College of Chest Physicians will hold its 23rd Annual Meeting at Hotel Commodore, New York City, May 29-June 2. Headquarters for the College is at 112 East Chestnut Street, Chicago 11, Ill.

The Third International Medical-Surgical Meetings will be held at the palace of "Torino-Esposizioni" in Torino, Italy, June 1-9, 1957.

Persons in the field of medical sciences

from all over the world will take part in the meetings. For further information address the Secretary General, Minverva Medica, Corso Bramante 83-85, Torino, Italy.

The 34th Annual Conference of the American Physical Therapy Association will be held at the Hotel Statler in Detroit, Mich., June 23-29. Further information may be obtained from that association the address of which is 1790 Broadway, New York 19, N.Y.

NERVE GAS FILM

A 30-minute color film, "Nerve Gas Casualties and Their Treatment," portraying the effects of nerve gas and the treatment of casualties, had its premiere showing in Washington, D.C., recently by the Federal Civil Defense Administration.

The film is sponsored by E. R. Squibb & Sons, and was produced with the cooperation of FCDA by the Audio Productions, Inc., New York. It will be available for local showings to professional organizations. Arrangements should be made with the Federal Civil Defense Administration, Battle Creek, Mich.

BROCHURE AVAILABLE

The Medical Witness, a brochure offering expert guidance to physicians on the presentation of medical testimony, is now available from the Wm. S. Merrell Company, Cincinnati, by writing to the Director of Professional Relations, that company, Cincinnati 15, Ohio.

SOMETHING NEW

Blood urea can be tested with 0.2 cc blood taken from the finger tip by means of a new blood urea test kit which is now on the market.

A new and safer rabies vaccine, produced in embryonated duck eggs, is now available to physicians. It has been shown in tests to be free of a "paralytic factor" that sometimes has caused paralysis and death during rabies treatment. The vaccine is said to be "doubly safe" since the virus used in making it is of a strain which is nonvirulent in man and is treated with a chemical which kills the virus but does not interfere with its antigenicity. The vaccine is produced by Eli Lilly and Company.

Honor Roll

Since the publication of our last list, the following sponsored one or more applicants for membership in the Association:

CWO Robert A. Barnhart, U. S. Army
Major Edward A. Barrett, MC, USAR
Capt. Lester J. Besen, USAF (MC)
Capt. Leon A. Bowden, MSC, Ill. NG
Capt. Samuel Candel, MC, USNR
Capt. R. F. Carmody (MC), USN
Lt. Col. John S. Chain, MC, USAR
Major John R. Daniels, MC, USA
Col. Sterrett E. Dietrich, MC, USA
Col. Bryan C. T. Fenton, MC, USA
Major Gen. Alvin L. Gorby, MC, USA
Col. Jos. Hass, MC, AUS
Capt. Barbara Hodgkins, USAF (MSpC)
Lt. Col. Wiley H. Horn, VC, USA
Capt. E. V. Jobe (MC), USN
Col. Robert C. Kimberly, MC, Md. NG
Col. Amos R. Koontz, MC, Md. NG
David Kramish, M.D.
Capt. H. Easton McMahon, MC, USNR
Gerardo H. Martinez, M.D.
Hugh B. Mitchell, M.D.
Dr. Irving Nachamie
Dr. E. T. Odom
Major Alois Peczenik, MC, USA
Sr. Dent. Surg. Wm. J. Pennoyer, USPHS
Capt. Roger L. Rothrock, MSC, USAR
Dr. Eric A. Sailer
Capt. John R. Seal (MC), USN
Capt. Wm. M. Silliphant (MC), USN
Lt. Col. Bernard Skold, VC, USA
Perry C. Smith, M.D.
Col. Walter H. Stevenson, MC, USA
Dr. Elmer C. Texter, Sr.
Capt. Jose M. Vidal Yebra, MC, Cuban Army

OBITUARIES

Col. Humphrey N. Ervin, U. S. Army, Ret.

Humphrey N. Ervin, Colonel, U. S. Army, Retired, died at Springfield, Virginia, January 6, at the age of 73.

Colonel Ervin was a native of Kentucky. He received his medical degree from the University of Cincinnati in 1912. In August 1917 he entered the active military service and was retired in 1947. He was a member of the Association of Military Surgeons since 1917.

Capt. Frank L. Pleadwell, U. S. Navy, Ret.

Frank Lester Pleadwell, Captain, U. S. Navy, Retired, died at Tripler Army Hospital, January 30, at the age of 83.

Captain Pleadwell was a native of Massachusetts and was graduated from Harvard University Medical School in 1896. He was appointed Assistant Surgeon in the Medical Corps of the Navy and entered the Naval service on October 24, 1896. He was retired on December 23, 1929. He was president of our Association in 1922.

He is survived by his wife, Laura Pleadwell, 1522-C Alema Drive, Honolulu, T.H.

Interment was at Arlington National Cemetery.

Col. Douglas F. Duvall, U. S. Army, Ret.

Douglas F. Duvall, Colonel, U. S. Army, Retired, died at Annapolis, Maryland, January 16 at the age of 87.

He was a native of Maryland, and received his medical degree from the University of Virginia in 1894. He entered military service in 1898 and was retired in June 1934, having reached the statutory age for retirement at that time.

Colonel Duvall had been a member of the Association of Military Surgeons since 1909.

Dr. Ollie J. B. Bennett

Ollie Josephine Baird Bennett, M. D., died at her home in Alexandria, Va., on February 4 at the age of 84.

She was one of the first five women doctors to serve in the Army Medical Corps. A first lieutenant in World War I, she instructed more than 200 nurses and enlisted men in anesthesia at Camp McClellan, Alabama.

Doctor Bennett was born in Decatur, Illinois, and received her medical degree from Boston University Medical School. She is survived by her daughter, Mrs. Olive Prescott Digges of Newport News, Va.

BOOK REVIEWS

STUDIES IN TOPECTOMY. Edited by Nolan D. C. Lewis, M.D., Carney Landis, Ph.D., D.Sc., and H. E. King, Ph.D. A report of the New York Brain Research Project. 248 pages. Grune & Stratton, New York and London. 1956. Price $6.75.

This text is a monograph describing a series of studies constituting the report of the activities of the New York State Associates in Brain Research between June 1948, and April 1949. This group of investigators was formed to explore the potentialities of psychosurgical methods as a therapy for mental disorder, and to investigate the role of the frontal lobes of the brain in human behavior. The current report is, in some degree, a continuation of two previous reports published by the Columbia-Greystone Associates. This monograph is to be considered an interim study, based primarily on the first two years of observations made by the New York State Group, whose main aim it is to apply previous findings to larger groups of clinical material.

The chapters are written by a combination of neurosurgeons, psychiatrists, neurologists, psychologists, and sociologists, and are approached from the standpoint of surgical procedures, physiological effects, vestibular functions, psychometric studies, general activity, psychopathology, sexual behavior, late psychiatric effects, and social adequacy upon return to their hospital or home. The material is well presented. The monograph, itself, is a valuable addition to the field of psychosurgery, but must be considered only a further chapter in prior reports and integrated into the other literature on this subject. The investigators reporting are all of considerable stature and experience. The results are presented as an increase in empirical observations, both positive and negative, in relation to the problem of psychosurgery in the human, non-diseased brain with a stated hope that such facts will lead to new knowledge that will be meaningful, and change our current void as quoted from the first Columbia-Greystone Report—"No existing theory or hypothesis dealing with the psychologic significance of the human frontal lobes is tenable." They are to be congratulated on their conscientious effort to avoid overgeneralizations, their awareness of the lack of basic knowledge, and not succumbing to indiscriminately relating the findings of any one discipline to all related fields. The text is recommended for specialists and research workers in the various fields concerned, and is not one for the casual reader.

LT. COL. JAMES F. HAMMILL, MC, USA

PRACTITIONER'S CONFERENCES—HELD AT NEW YORK HOSPITAL—CORNELL MEDICAL CENTER. VOLUME IV. Edited by Claude E. Forkner, M.D., F.A.C.P., Professor of Clinical Medicine, Cornell University Medical College—407 pages. Appleton-Century-Crofts, Inc., New York. 1956. Price $6.50.

This series of clinical conferences represents a continuation of the past custom of publishing the results of their regularly held meetings at this well known teaching center. These are bedside teaching clinics pointed towards a definite subject and stressing basic factors, recent advances, common errors or points of controversy. A different panel of well known experts conducts each session and audience participation is encouraged. They are exceptionally well written and easy to read.

The topics are usually the more commonly encountered problems such as: pulmonary hypertension, hypo- and hyperthyroidism, fractures of the hips, mechanism of therapy of the anemias, burns, obesity, ileitis, homosexuality, cancer of the rectum and anus, patent ductus arteriosus and coarctation of the aorta, rheumatic heart disease, and pinworm infestation. In reading these, one gets the feeling of a live clinic, that is, the patient and the discussers seem to be with you in the same room. The problems are more practical and very well stressed, ending with a summary by Dr. Forkner which firms up the thoughts in one's mind.

This volume is highly recommended to all busy practitioners, interns and residents as a means of continuing their graduate education. It is stimulating and authoritative, yet takes little time to read.

CAPT. LESTER J. POPE, MC, USN

NEW BOOKS

The Physician-Writer's Book—Tricks of the Trade of Medical Writing, By Richard M. Hewitt, A.M., M.D., W. B. Saunders Co., Philadelphia, Pa. Price $9.00.

Pediatric Cardiology, by Alexander S. Nadas, M.D., F.A.A.P. W. B. Saunders Co., Philadelphia, Pa. Price $12.00.

Clinical Use of Radioisotopes, by Wm. H. Bierwaltes, M.D., Philip C. Johnson, M.D., and Arthur J. Solari, B.S., M.S. W. B. Saunders Co., Philadelphia, Pa. Price $11.50.

Anesthesia for Surgery of the Heart, by Kenneth K. Keown, M.D. Charles C Thomas, Publisher. Springfield, Ill. Price $3.75.

The Principles and Art of Plastic Surgery, by Sir Harold Gillies and D. Ralph Millard, Jr. Little, Brown & Co., Boston, Mass. Two Volumes, Price $35.00.

Chirurgie Orthopedique des Paralysies, by R. Merle D'Aubigne, J. Benassy, and J. O. Ramadier. Masson et Cie, Editeurs, Paris, France. Price: Broche 4,200 fr.; Cartonne toile: 5,000 fr.

Practical Dermatology, by Samuel M. Peck, B.S., M.D. and Laurence L. Palitz, M.D., Ph.D. McGraw-Hill Book Co., Inc., New York, N.Y. Price $7.00.

Drugs in Current Use, 1957, edited by Walter Modell, M.D. Springer Publishing Co., New York, N.Y. Price $2.00.

Dorland's Illustrated Medical Dictionary, New (23rd) Edition, W. B. Saunders Co., Philadelphia, Pa. Price $12.50.

Venoms, edited by Eleanor E. Buckley and Nander Porges. American Association for the Advancement of Science, Washington 5, D.C. Price $8.25.

Oral Cancer and Tumors of the Jaws, by George S. Sharp, Weldon K. Bullock, and John W. Hazler. The Blakiston Division, McGraw-Hill Book Co., New York, N.Y. Price $15.00.

Ultramicro Methods for Clinical Laboratories, by Edwin M. Knights, Jr., M.D., Roderick P. MacDonald, Ph.D., and Jaan Ploompuu. Grune & Stratton, Inc., New York, N.Y. Price $4.75.

Proceedings of the Third National Cancer Conference, Detroit, Mich. June 4-6, 1956. J. B. Lippincott Co., Philadelphia, Pa. Price $9.00.

Principles and Technics of Rehabilitation, Florence Jones Terry, Gladys S. Benz, Dorothy Mereness, and Frank R. Kleffner. Deborah MacLurg Jensen, Editor. The C. V. Mosby Co., St. Louis, Mo. Price $5.50.

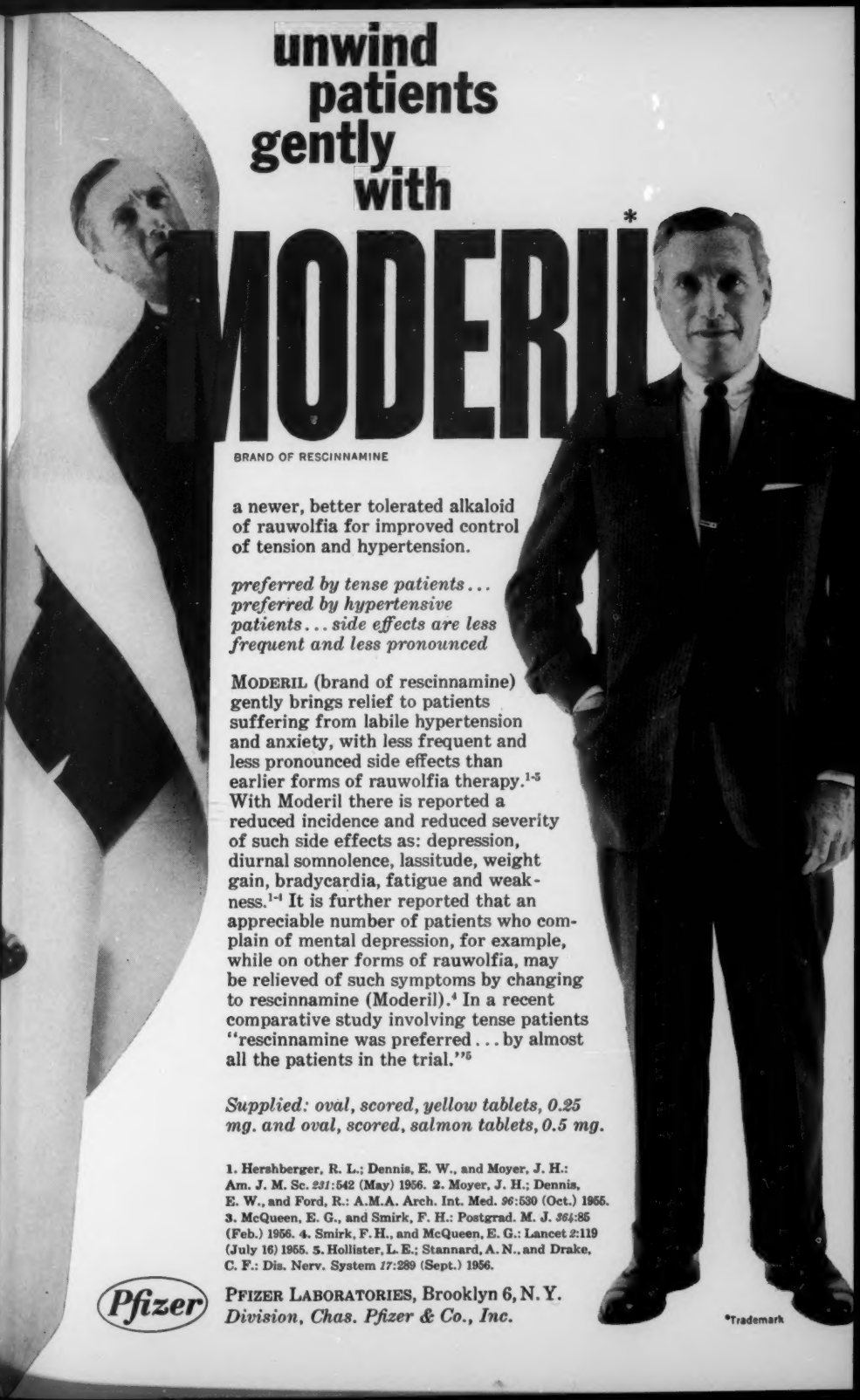
From Witchcraft to World Health, by S. & V. Leff. The Macmillan Co. New York, N.Y. Price $4.50.

Handbook of Differential Diagnosis, 2nd ed., by Harold Thomas Hyman, M.D. J. B. Lippincott Co., Philadelphia, Pa. Price $8.00.

Bulletin of the World Health Organization. *Malaria.* World Health Organization, Geneva. Price $6.00.

Clinical Physiology. The Functional Pathology of Disease, edited by Arthur Grollman, M.D. McGraw-Hill Book Co., Inc., New York, N.Y. Price $12.50.

Current Therapy, 1957, edited by Howard F. Conn, M.D. W. B. Saunders Co., Philadelphia, Pa. Price $11.00.


unwind
patients
gently
with
MODERIL*
BRAND OF RESCINNAMINE
a newer, better tolerated alkaloid of rauwolfia for improved control of tension and hypertension.
preferred by tense patients... preferred by hypertensive patients... side effects are less frequent and less pronounced
MODERIL (brand of rescinnamine) gently brings relief to patients suffering from labile hypertension and anxiety, with less frequent and less pronounced side effects than earlier forms of rauwolfia therapy.[1-5] With Moderil there is reported a reduced incidence and reduced severity of such side effects as: depression, diurnal somnolence, lassitude, weight gain, bradycardia, fatigue and weakness.[1-4] It is further reported that an appreciable number of patients who complain of mental depression, for example, while on other forms of rauwolfia, may be relieved of such symptoms by changing to rescinnamine (Moderil).[4] In a recent comparative study involving tense patients "rescinnamine was preferred... by almost all the patients in the trial."[5]
Supplied: oval, scored, yellow tablets, 0.25 mg. and oval, scored, salmon tablets, 0.5 mg.
1. Hershberger, R. L.; Dennis, E. W., and Moyer, J. H.: Am. J. M. Sc. *231*:542 (May) 1956. 2. Moyer, J. H.; Dennis, E. W., and Ford, R.: A.M.A. Arch. Int. Med. *96*:530 (Oct.) 1955. 3. McQueen, E. G., and Smirk, F. H.: Postgrad. M. J. *364*:85 (Feb.) 1956. 4. Smirk, F. H., and McQueen, E. G.: Lancet *2*:119 (July 16) 1955. 5. Hollister, L. E.; Stannard, A. N., and Drake, C. F.: Dis. Nerv. System *17*:289 (Sept.) 1956.
Pfizer
PFIZER LABORATORIES, Brooklyn 6, N.Y.
Division, Chas. Pfizer & Co., Inc.
*Trademark

The Association of Military Surgeons of the United States

Founded 1891 Incorporated by Act of Congress 1903
Suite 718, New Medical Bldg., 1726 Eye Street, N.W., Washington 6, D.C.
Telephone NAtional 8-2206
Official Journal: MILITARY MEDICINE

OFFICERS—1957

President:
COLONEL AMOS R. KOONTZ
MC, Md., NG

First Vice-President:
COL. CHARLES R. MUELLER
U. S. Army, Ret. (VA)

Second Vice-President:
BRIG. GEN. H. H. TWITCHELL
U. S. Air Force (MC)

Third Vice-President:
MAJ. GEN. WALLACE H. GRAHAM
U. S. Air Force Res. (MC)

Fourth Vice-President:
JOHN W. CRONIN
Ass't. Surg. Gen. USPHS

Fifth Vice-President:
MAJ. GEN. JAMES P. COONEY
MC, U. S. Army

Sixth Vice-President:
REAR ADM. IRWIN L. NORMAN
MC, U.S. Navy

Secretary:
COL. ROBT. E. BITNER
U. S. Army, Ret.

Editor:
COL. ROBT. E. BITNER
U. S. Army, Ret.

Dental Section Chairman:
BRIG. GEN. L. C. FAIRBANK
U. S. Army, Ret.

Veterinary Section Chairman:
BRIG. GEN. J. A. MCCALLAM
U. S. Army, Ret.

M. S. C. Section Chairman:
COL. BERNARD AABEL
MSC, U.S. Army

Nurse Corps Section Chairman:
MISS RUTH L. JOHNSON
Nurse Div., USPHS

Medical Specialist Corps Section Chairman:
MISS ELEANOR G. LOOMIS
USPHS

Chapter Section Chairman:
CAPT. H. EASTON MCMAHON
MC, USNR

Executive Secretary:
STUART E. WOMELDORPH, D.C.L.

EXECUTIVE COUNCIL

The Officers and:

REAR ADM. THOMAS F. COOPER, MC, USN
MAJ. GEN. PAUL I. ROBINSON, MC, USA
MAJ. GEN. OLIN F. MCILNAY, USAF (MC)
BRIG. GEN. FRANK E. WILSON, MC, USAR
COL. WM. S. MIDDLETON, MC, USAR (VA)
THOMAS A. FOSTER, Pharm. Dir. USPHS
COL. EDMUND G. BEACHAM, MC, Md., NG

BOARD OF TRUSTEES, RETIREMENT FUND

BRIG. GEN. L. C. FAIRBANK, USA, Ret., Pres. BRIG. GEN. C. M. WALSON, USA, Ret, Treas.
JAMES P. LEAKE, Med. Dir. USPHS, Ret., Secretary

LIVING PAST PRESIDENTS

(Rank held at time of office)

ASST. SURG. GEN. JOHN W. KERR, USPHS (1921)
COL. FREDERICK H. VINUP, MC, Md., NG (1928)
COL. CHARLES W. COMFORT, MC, Conn. NG (1932)
ASST. SURG. GEN. RALPH C. WILLIAMS, USPHS (1933)
REAR ADM. PERCEVAL S. ROSSITER, MC, USN (1937)
SURG. GEN. THOMAS PARRAN, USPHS (1939)
MAJ. GEN. CHARLES R. REYNOLDS, MC, USA (1940)
COL. JAMES A. MATTISON, Vet. Adm. (1942)
COL. LUCIUS A. SALISBURY, MC, N.Y., NG (1944)
ASST. SURG. GEN. WARREN F. DRAPER, USPHS (1947)
VICE ADM. JOEL T. BOONE, MC, USN (1949)
COL. WILLIAM H. TRIPLETT, MC, Md., NG (1950)
COL. ROBERT C. COOK, MC, AUS, Vet. Adm. (1951)
MAJ. GEN. HARRY G. ARMSTRONG, USAF (MC) (1952)
REAR ADM. WINCHELL MCK. CRAIG, MC, USNR (1953)
SURG. GEN. LEONARD A. SCHEELE, USPHS (1954)*
MAJ. GEN. JOSEPH I. MARTIN, MC, USA (1955)*
REAR ADM. W. DANA, MC, USN (1956)*
*Member Sinking Fund Committee